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(54) Title: PLANT CELLULOSE SYNTHASES

(57) Abstract

This invention relates to an isolated nucleic acid fragment encoding a cellulose synthase. The invention also relates to the construction of a chimeric gene encoding all or a portion of the cellulose synthase, in sense or antisense orientation, wherein expression of the chimeric gene results in production of altered levels of the cellulose synthase in a transformed host cell.

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             1                                                          60
SEQ ID NO:2  ------------------------------------------------------------
SEQ ID NO:4  RAAQAQRNKGKPQPEEQKLASVSLP--LPHSRFIPTPPRRRYRRR---RTHACPG----I
SEQ ID NO:6  ------------------------------------------------------------
SEQ ID NO:8  HSSYTKSRSSLAQPRAAPRQAQPPP--ATAACACERSPRPGDQRRGGLRAFRCAAAAGFV
SEQ ID NO:10 ------------------------------------------------------------
SEQ ID NO:12 RCS---RRWTCSSPPPTPTRSRRSPRRTP-------------------------------
SEQ ID NO:14 ------------------------------------------------------------
SEQ ID NO:16 ------------------------------------------------------------
SEQ ID NO:18 ------------------------------------------------------------
SEQ ID NO:20 ------------------------------------------------------------
SEQ ID NO:22 ------------------------------------------------------------
SEQ ID NO:23 ------------------------------------------------------------
SEQ ID NO:24 MNTGGR------------------------------------------------------
SEQ ID NO:25 ------------------------------------------------------------
SEQ ID NO:26 MASTPPQTSKKVRNNSGSGQTVKFARRTSSGRYVSLS-RDNIELSGELSGDYSNYTVHIP
SEQ ID NO:27 ------------------------------------------------------------
SEQ ID NO:28 ------------------------------------------------------------
SEQ ID NO:29 R---PR------------------------------------------------------

             61                                                        120
SEQ ID NO:2  ------------------------------------------------------------
SEQ ID NO:4  W-RSGSARG----ME-ASAGLVAGSHNRNELV-VIRRDGEPGPKP--MDQRNGQVCQI--
SEQ ID NO:6  ------------------------------------------------------------
SEQ ID NO:8  RERDPAGRGGGPEME-ASAGLVAGSHNRNELV-VIRRDRESGAAGGGAARRAEAPCQI--
SEQ ID NO:10 -------------ME-ASAGLVAGSHNRNELV-VIRRDGDPGPKP--PREQNGQVCQI--
SEQ ID NO:12 -------------------------------------------------------C----
SEQ ID NO:14 -------------ME-ASAGLVAGSHNRNELV-VIHGHEEP--KA--LKNLDGQVCEI--
SEQ ID NO:16 ------------------------------------------------------------
SEQ ID NO:18 ------------------------------------------------------------
SEQ ID NO:20 ------------------------------------------------------------
SEQ ID NO:22 ------------------------------------------------------------
SEQ ID NO:23 -------------ME-ASAGLVAGSYRRNELV-RIRHESDGGTKP--LKNMNGQICQI--
SEQ ID NO:24 --------------------LIAGSHNRNEFV-LI--NADESARIRSVQELSGQTCQI--
SEQ ID NO:25 ------------------------------------------------------------
SEQ ID NO:26 PTPDNQPMATKAEEQYVSNSLFTGGFNSVTRAHLMDKVIDSDVTHPQMAGAKGSSCAMPA
SEQ ID NO:27 -------------ME-ASAGLVAGSHNRNELV-VIHNHEEP--KP--LKNLDGQFCEI--
SEQ ID NO:28 ------------------------------------------------------------
SEQ ID NO:29 --------------------LIAGSHNRNEFV-LI--NADENARIRSVQELSGQTCQI--

             121                                                       180
SEQ ID NO:2  ------------------------------------------------------------
SEQ ID NO:4  CGDDVGRNPDGEPFVACNECAFPICRDCYEYERREGTQNCPQCKTRFKRLKGCARVPGD-
SEQ ID NO:6  ------------------------------------------------------------
SEQ ID NO:8  CGDEVGVGFDGEPFVACNECAFPVCRACYEYERREGSQACPQCRTRYKRLKGCPRVAGD-
SEQ ID NO:10 CGDDVGLAPGGDPFVACNECAFPVCRDCYEYERREGTQNCPQCKTRYKRLKGCQRVTGD-
SEQ ID NO:12 ------------------CPY---------------------------------------
SEQ ID NO:14 CGDGVGLTVDGDLFVACNECGFPVCRPCYEYERREGSHLCPQCKTRYKRLKGSPRVEGDD
SEQ ID NO:16 ------------------------------------------------------------
SEQ ID NO:18 ------------------------------------------------------------
SEQ ID NO:20 ------------------------------------------------------------
SEQ ID NO:22 ------------------------------------------------------------
SEQ ID NO:23 CGDDVGLAETGDVFVACNECAFPVCRPCYEYERKDGTQCCPQCKTRFRRHRGSPRVEGDE
SEQ ID NO:24 CGDEIELTVSSELFVACNECAFPVCRPCYEYERREGNQACPQCKTRYKRIKGSPRVDGDD
SEQ ID NO:25 ------------------------------------------------------------
SEQ ID NO:26 CDGNVMKDERGKDVMPC-ECRFKICRDCFMDAQKE-TGLCPGCKEQYK------------
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Jinrui Shi
Serial No. 10/042,894

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VN	Viet Nam
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ZW	Zimbabwe

TITLE

PLANT CELLULOSE SYNTHASES

This application claims the benefit of U.S. Provisional Application No. 60/092,844, filed July 14, 1998.

FIELD OF THE INVENTION

This invention is in the field of plant molecular biology. More specifically, this invention pertains to nucleic acid fragments encoding cellulose biosynthetic enzymes in plants and seeds.

BACKGROUND OF THE INVENTION

Cellulose is a major component of plant fiber, e.g. cotton fiber. Cellulose is composed of crystalline beta-1,4-glucan microfibrils (see World Patent Publication No. WO 98/00549). These microfibrils are strong and can resist enzymatic and mechanical degradation and are important in determining nutritional quality of animal and human foodstuffs. Hence, modification of the biosynthetic pathway responsible for cellulose synthesis through modification of cellulose synthase activity could potentially alter fiber quantity, either by producing more or less fiber in a particular plant species or in a specific organ or tissue of a particular plant. Modification of cellulose synthase activity could increase the value of the fiber to the end-user and may improve the structural integrity of the plant cell wall. Lastly, because cellulose is a major cell wall component, inhibition of cellulose synthesis would probably be lethal. Thus, cellulose synthase may serve as the target for a novel class of herbicides. Plant cellulose synthase genes, homologs of the bacterial celA genes encoding the catalytic subunit of cellulose synthase, have been reported from cotton, *Arabidopsis*, rice and alfala (World Patent Publication Nos. WO 98/00549 and WO 98/18949).

There is a great deal of interest in identifying the genes that encode proteins involved in cellulose synthesis. These genes may be used in plant cells to control the synthesis of cellulose. Accordingly, the availability of nucleic acid sequences encoding all or a portion of a cellulose synthase would facilitate studies to better understand cellulose synthesis in plants and provide genetic tools to alter cellulose production.

SUMMARY OF THE INVENTION

The instant invention relates to isolated nucleic acid fragments encoding cellulose biosynthesis enzymes. Specifically, this invention concerns an isolated nucleic acid fragment encoding a cellulose synthase and an isolated nucleic acid fragment that is substantially similar to an isolated nucleic acid fragment encoding a cellulose synthase. In addition, this invention relates to a nucleic acid fragment that is complementary to the nucleic acid fragment encoding cellulose synthase. An additional embodiment of the instant invention pertains to a polypeptide encoding all or a substantial portion of a cellulose synthase.

In another embodiment, the instant invention relates to a chimeric gene encoding a cellulose synthase, or to a chimeric gene that comprises a nucleic acid fragment that is complementary to a nucleic acid fragment encoding a cellulose synthase, operably linked to suitable regulatory sequences, wherein expression of the chimeric gene results in production of levels of the encoded protein in a transformed host cell that is altered (i.e., increased or decreased) from the level produced in an untransformed host cell.

In a further embodiment, the instant invention concerns a transformed host cell comprising in its genome a chimeric gene encoding a cellulose synthase, operably linked to suitable regulatory sequences. Expression of the chimeric gene results in production of altered levels of the encoded protein in the transformed host cell. The transformed host cell can be of eukaryotic or prokaryotic origin, and include cells derived from higher plants and microorganisms. The invention also includes transformed plants that arise from transformed host cells of higher plants, and seeds derived from such transformed plants.

An additional embodiment of the instant invention concerns a method of altering the level of expression of a cellulose synthase in a transformed host cell comprising: a) transforming a host cell with a chimeric gene comprising a nucleic acid fragment encoding a cellulose synthase; and b) growing the transformed host cell under conditions that are suitable for expression of the chimeric gene wherein expression of the chimeric gene results in production of altered levels of cellulose synthase in the transformed host cell.

An addition embodiment of the instant invention concerns a method for obtaining a nucleic acid fragment encoding all or a substantial portion of an amino acid sequence encoding a cellulose synthase.

A further embodiment of the instant invention is a method for evaluating at least one compound for its ability to inhibit the activity of a cellulose synthase, the method comprising the steps of: (a) transforming a host cell with a chimeric gene comprising a nucleic acid fragment encoding a cellulose synthase, operably linked to suitable regulatory sequences; (b) growing the transformed host cell under conditions that are suitable for expression of the chimeric gene wherein expression of the chimeric gene results in production of cellulose synthase in the transformed host cell; (c) optionally purifying the cellulose synthase expressed by the transformed host cell; (d) treating the cellulose synthase with a compound to be tested; and (e) comparing the activity of the cellulose synthase that has been treated with a test compound to the activity of an untreated cellulose synthase, thereby selecting compounds with potential for inhibitory activity.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE DESCRIPTIONS

The invention can be more fully understood from the following detailed description and the accompanying drawings and Sequence Listing which form a part of this application.

Figure 1 shows a comparison of the amino acid sequences set forth in SEQ ID NOs:2, 4, 8, 10, 12, 14, 16, 18, 20 and 22 and the *Arabidopsis thaliana* sequences (SEQ ID NOs:23 (gi 2827139), 24 (gi 2827141), 26 (gi 4467125), 27 (gi 4886756) and 29 (gi 3135611)) and *Gossypium hirsutum* sequences (SEQ ID NOs:25 (gi 1706958) and 28 (gi 5081779)).

Table 1 lists the polypeptides that are described herein, the designation of the cDNA clones that comprise the nucleic acid fragments encoding polypeptides representing all or a substantial portion of these polypeptides, and the corresponding identifier (SEQ ID NO:) as used in the attached Sequence Listing. The sequence descriptions and Sequence Listing attached hereto comply with the rules governing nucleotide and/or amino acid sequence disclosures in patent applications as set forth in 37 C.F.R. §1.821-1.825.

TABLE 1

Cellulose Biosynthetic Enzymes

Protein	Clone Designation	SEQ ID NO: (Nucleotide)	SEQ ID NO: (Amino Acid)
Cellulose Synthase	bsh1.pk0002.f6	1	2
Cellulose Synthase	Contig composed of: cco1n.pk0005.g3 cdt2c.pk002.g1 cdt2c.pk002.l16 csc1c.pk002.i1 p0031.ccmar05rb p0110.cgsma57r	3	4
Cellulose Synthase	cr1n.pk0135.e10	5	6
Cellulose Synthase	p0097.cqrad17rc	7	8
Cellulose Synthase	p0122.ckamh70rc	9	10
Cellulose Synthase	rlr24.pk0073.g1	11	12
Cellulose Synthase	sdp2c.pk005.o22	13	14
Cellulose Synthase	ses8w.pk0028.f3	15	16
Cellulose Synthase	ssl.pk0036.c10	17	18
Cellulose Synthase	Contig composed of: wl1.pk0009.c9 wr1.pk0160.d11 wre1n.pk0043.f9 wre1n.pk0043.h8 wre1n.pk0131.g10	19	20
Cellulose Synthase	wl1n.pk0044.b1	21	22

The Sequence Listing contains the one letter code for nucleotide sequence characters and the three letter codes for amino acids as defined in conformity with the IUPAC-IUBMB standards described in *Nucleic Acids Research 13*:3021-3030 (1985) and in the *Biochemical Journal 219 (No. 2)*:345-373 (1984) which are herein incorporated by reference. The

symbols and format used for nucleotide and amino acid sequence data comply with the rules set forth in 37 C.F.R. §1.822.

DETAILED DESCRIPTION OF THE INVENTION

In the context of this disclosure, a number of terms shall be utilized. As used herein, a "nucleic acid fragment" is a polymer of RNA or DNA that is single- or double-stranded, optionally containing synthetic, non-natural or altered nucleotide bases. A nucleic acid fragment in the form of a polymer of DNA may be comprised of one or more segments of cDNA, genomic DNA or synthetic DNA.

As used herein, "contig" refers to a nucleotide sequence that is assembled from two or more constituent nucleotide sequences that share common or overlapping regions of sequence homology. For example, the nucleotide sequences of two or more nucleic acid fragments can be compared and aligned in order to identify common or overlapping sequences. Where common or overlapping sequences exist between two or more nucleic acid fragments, the sequences (and thus their corresponding nucleic acid fragments) can be assembled into a single contiguous nucleotide sequence.

As used herein, "substantially similar" refers to nucleic acid fragments wherein changes in one or more nucleotide bases results in substitution of one or more amino acids, but do not affect the functional properties of the polypeptide encoded by the nucleotide sequence. "Substantially similar" also refers to nucleic acid fragments wherein changes in one or more nucleotide bases does not affect the ability of the nucleic acid fragment to mediate alteration of gene expression by gene silencing through for example antisense or co-suppression technology. "Substantially similar" also refers to modifications of the nucleic acid fragments of the instant invention such as deletion or insertion of one or more nucleotides that do not substantially affect the functional properties of the resulting transcript vis-à-vis the ability to mediate gene silencing or alteration of the functional properties of the resulting protein molecule. It is therefore understood that the invention encompasses more than the specific exemplary nucleotide or amino acid sequences and includes functional equivalents thereof.

For example, it is well known in the art that antisense suppression and co-suppression of gene expression may be accomplished using nucleic acid fragments representing less than the entire coding region of a gene, and by nucleic acid fragments that do not share 100% sequence identity with the gene to be suppressed. Moreover, alterations in a nucleic acid fragment which result in the production of a chemically equivalent amino acid at a given site, but do not effect the functional properties of the encoded polypeptide, are well known in the art. Thus, a codon for the amino acid alanine, a hydrophobic amino acid, may be substituted by a codon encoding another less hydrophobic residue, such as glycine, or a more hydrophobic residue, such as valine, leucine, or isoleucine. Similarly, changes which result in substitution of one negatively charged residue for another, such as aspartic acid for

glutamic acid, or one positively charged residue for another, such as lysine for arginine, can also be expected to produce a functionally equivalent product. Nucleotide changes which result in alteration of the N-terminal and C-terminal portions of the polypeptide molecule would also not be expected to alter the activity of the polypeptide. Each of the proposed modifications is well within the routine skill in the art, as is determination of retention of biological activity of the encoded products.

Moreover, substantially similar nucleic acid fragments may also be characterized by their ability to hybridize, under stringent conditions (0.1X SSC, 0.1% SDS, 65°C), with the nucleic acid fragments disclosed herein.

Substantially similar nucleic acid fragments of the instant invention may also be characterized by the percent identity of the amino acid sequences that they encode to the amino acid sequences disclosed herein, as determined by algorithms commonly employed by those skilled in this art. Preferred are those nucleic acid fragments whose nucleotide sequences encode amino acid sequences that are 80% identical to the amino acid sequences reported herein. More preferred nucleic acid fragments encode amino acid sequences that are 90% identical to the amino acid sequences reported herein. Most preferred are nucleic acid fragments that encode amino acid sequences that are 95% identical to the amino acid sequences reported herein. Sequence alignments and percent identity calculations were performed using the Megalign program of the LASARGENE bioinformatics computing suite (DNASTAR Inc., Madison, WI). Multiple alignment of the sequences was performed using the Clustal method of alignment (Higgins and Sharp (1989) *CABIOS. 5*:151-153) with the default parameters (GAP PENALTY=10, GAP LENGTH PENALTY=10). Default parameters for pairwise alignments using the Clustal method were KTUPLE 1, GAP PENALTY=3, WINDOW=5 and DIAGONALS SAVED=5.

A "substantial portion" of an amino acid or nucleotide sequence comprises an amino acid or a nucleotide sequence that is sufficient to afford putative identification of the protein or gene that the amino acid or nucleotide sequence comprises. Amino acid and nucleotide sequences can be evaluated either manually by one skilled in the art, or by using computer-based sequence comparison and identification tools that employ algorithms such as BLAST (Basic Local Alignment Search Tool; Altschul et al. (1993) *J. Mol. Biol. 215*:403-410; see also www.ncbi.nlm.nih.gov/BLAST/). In general, a sequence of ten or more contiguous amino acids or thirty or more contiguous nucleotides is necessary in order to putatively identify a polypeptide or nucleic acid sequence as homologous to a known protein or gene. Moreover, with respect to nucleotide sequences, gene-specific oligonucleotide probes comprising 30 or more contiguous nucleotides may be used in sequence-dependent methods of gene identification (e.g., Southern hybridization) and isolation (e.g., *in situ* hybridization of bacterial colonies or bacteriophage plaques). In addition, short oligonucleotides of 12 or more nucleotides may be used as amplification primers in PCR in order to obtain a particular

nucleic acid fragment comprising the primers. Accordingly, a "substantial portion" of a nucleotide sequence comprises a nucleotide sequence that will afford specific identification and/or isolation of a nucleic acid fragment comprising the sequence. The instant specification teaches amino acid and nucleotide sequences encoding polypeptides that comprise one or more particular plant proteins. The skilled artisan, having the benefit of the sequences as reported herein, may now use all or a substantial portion of the disclosed sequences for purposes known to those skilled in this art. Accordingly, the instant invention comprises the complete sequences as reported in the accompanying Sequence Listing, as well as substantial portions of those sequences as defined above.

"Codon degeneracy" refers to divergence in the genetic code permitting variation of the nucleotide sequence without effecting the amino acid sequence of an encoded polypeptide. Accordingly, the instant invention relates to any nucleic acid fragment comprising a nucleotide sequence that encodes all or a substantial portion of the amino acid sequences set forth herein. The skilled artisan is well aware of the "codon-bias" exhibited by a specific host cell in usage of nucleotide codons to specify a given amino acid. Therefore, when synthesizing a nucleic acid fragment for improved expression in a host cell, it is desirable to design the nucleic acid fragment such that its frequency of codon usage approaches the frequency of preferred codon usage of the host cell.

"Synthetic nucleic acid fragments" can be assembled from oligonucleotide building blocks that are chemically synthesized using procedures known to those skilled in the art. These building blocks are ligated and annealed to form larger nucleic acid fragments which may then be enzymatically assembled to construct the entire desired nucleic acid fragment. "Chemically synthesized", as related to nucleic acid fragment, means that the component nucleotides were assembled *in vitro*. Manual chemical synthesis of nucleic acid fragments may be accomplished using well established procedures, or automated chemical synthesis can be performed using one of a number of commercially available machines. Accordingly, the nucleic acid fragments can be tailored for optimal gene expression based on optimization of nucleotide sequence to reflect the codon bias of the host cell. The skilled artisan appreciates the likelihood of successful gene expression if codon usage is biased towards those codons favored by the host. Determination of preferred codons can be based on a survey of genes derived from the host cell where sequence information is available.

"Gene" refers to a nucleic acid fragment that expresses a specific protein, including regulatory sequences preceding (5' non-coding sequences) and following (3' non-coding sequences) the coding sequence. "Native gene" refers to a gene as found in nature with its own regulatory sequences. "Chimeric gene" refers any gene that is not a native gene, comprising regulatory and coding sequences that are not found together in nature. Accordingly, a chimeric gene may comprise regulatory sequences and coding sequences that are derived from different sources, or regulatory sequences and coding sequences derived

from the same source, but arranged in a manner different than that found in nature. "Endogenous gene" refers to a native gene in its natural location in the genome of an organism. A "foreign" gene refers to a gene not normally found in the host organism, but that is introduced into the host organism by gene transfer. Foreign genes can comprise native genes inserted into a non-native organism, or chimeric genes. A "transgene" is a gene that has been introduced into the genome by a transformation procedure.

"Coding sequence" refers to a nucleotide sequence that codes for a specific amino acid sequence. "Regulatory sequences" refer to nucleotide sequences located upstream (5' non-coding sequences), within, or downstream (3' non-coding sequences) of a coding sequence, and which influence the transcription, RNA processing or stability, or translation of the associated coding sequence. Regulatory sequences may include promoters, translation leader sequences, introns, and polyadenylation recognition sequences.

"Promoter" refers to a nucleotide sequence capable of controlling the expression of a coding sequence or functional RNA. In general, a coding sequence is located 3' to a promoter sequence. The promoter sequence consists of proximal and more distal upstream elements, the latter elements often referred to as enhancers. Accordingly, an "enhancer" is a nucleotide sequence which can stimulate promoter activity and may be an innate element of the promoter or a heterologous element inserted to enhance the level or tissue-specificity of a promoter. Promoters may be derived in their entirety from a native gene, or be composed of different elements derived from different promoters found in nature, or even comprise synthetic nucleotide segments. It is understood by those skilled in the art that different promoters may direct the expression of a gene in different tissues or cell types, or at different stages of development, or in response to different environmental conditions. Promoters which cause a nucleic acid fragment to be expressed in most cell types at most times are commonly referred to as "constitutive promoters". New promoters of various types useful in plant cells are constantly being discovered; numerous examples may be found in the compilation by Okamuro and Goldberg (1989) *Biochemistry of Plants 15*:1-82. It is further recognized that since in most cases the exact boundaries of regulatory sequences have not been completely defined, nucleic acid fragments of different lengths may have identical promoter activity.

The "translation leader sequence" refers to a nucleotide sequence located between the promoter sequence of a gene and the coding sequence. The translation leader sequence is present in the fully processed mRNA upstream of the translation start sequence. The translation leader sequence may affect processing of the primary transcript to mRNA, mRNA stability or translation efficiency. Examples of translation leader sequences have been described (Turner and Foster (1995) *Molecular Biotechnology 3*:225).

The "3' non-coding sequences" refer to nucleotide sequences located downstream of a coding sequence and include polyadenylation recognition sequences and other sequences

encoding regulatory signals capable of affecting mRNA processing or gene expression. The polyadenylation signal is usually characterized by affecting the addition of polyadenylic acid tracts to the 3' end of the mRNA precursor. The use of different 3' non-coding sequences is exemplified by Ingelbrecht et al. (1989) *Plant Cell 1*:671-680.

"RNA transcript" refers to the product resulting from RNA polymerase-catalyzed transcription of a DNA sequence. When the RNA transcript is a perfect complementary copy of the DNA sequence, it is referred to as the primary transcript or it may be a RNA sequence derived from posttranscriptional processing of the primary transcript and is referred to as the mature RNA. "Messenger RNA (mRNA)" refers to the RNA that is without introns and that can be translated into polypeptide by the cell. "cDNA" refers to a double-stranded DNA that is complementary to and derived from mRNA. "Sense" RNA refers to an RNA transcript that includes the mRNA and so can be translated into a polypeptide by the cell. "Antisense RNA" refers to an RNA transcript that is complementary to all or part of a target primary transcript or mRNA and that blocks the expression of a target gene (see U.S. Patent No. 5,107,065, incorporated herein by reference). The complementarity of an antisense RNA may be with any part of the specific nucleotide sequence, i.e., at the 5' non-coding sequence, 3' non-coding sequence, introns, or the coding sequence. "Functional RNA" refers to sense RNA, antisense RNA, ribozyme RNA, or other RNA that may not be translated but yet has an effect on cellular processes.

The term "operably linked" refers to the association of two or more nucleic acid fragments on a single nucleic acid fragment so that the function of one is affected by the other. For example, a promoter is operably linked with a coding sequence when it is capable of affecting the expression of that coding sequence (i.e., that the coding sequence is under the transcriptional control of the promoter). Coding sequences can be operably linked to regulatory sequences in sense or antisense orientation.

The term "expression", as used herein, refers to the transcription and stable accumulation of sense (mRNA) or antisense RNA derived from the nucleic acid fragment of the invention. Expression may also refer to translation of mRNA into a polypeptide. "Antisense inhibition" refers to the production of antisense RNA transcripts capable of suppressing the expression of the target protein. "Overexpression" refers to the production of a gene product in transgenic organisms that exceeds levels of production in normal or non-transformed organisms. "Co-suppression" refers to the production of sense RNA transcripts capable of suppressing the expression of identical or substantially similar foreign or endogenous genes (U.S. Patent No. 5,231,020, incorporated herein by reference).

"Altered levels" refers to the production of gene product(s) in transgenic organisms in amounts or proportions that differ from that of normal or non-transformed organisms.

"Mature" protein refers to a post-translationally processed polypeptide; i.e., one from which any pre- or propeptides present in the primary translation product have been removed.

"Precursor" protein refers to the primary product of translation of mRNA; i.e., with pre- and propeptides still present. Pre- and propeptides may be but are not limited to intracellular localization signals.

A "chloroplast transit peptide" is an amino acid sequence which is translated in conjunction with a protein and directs the protein to the chloroplast or other plastid types present in the cell in which the protein is made. "Chloroplast transit sequence" refers to a nucleotide sequence that encodes a chloroplast transit peptide. A "signal peptide" is an amino acid sequence which is translated in conjunction with a protein and directs the protein to the secretory system (Chrispeels (1991) *Ann. Rev. Plant Phys. Plant Mol. Biol. 42*:21-53). If the protein is to be directed to a vacuole, a vacuolar targeting signal (*supra*) can further be added, or if to the endoplasmic reticulum, an endoplasmic reticulum retention signal (*supra*) may be added. If the protein is to be directed to the nucleus, any signal peptide present should be removed and instead a nuclear localization signal included (Raikhel (1992) *Plant Phys. 100*:1627-1632).

"Transformation" refers to the transfer of a nucleic acid fragment into the genome of a host organism, resulting in genetically stable inheritance. Host organisms containing the transformed nucleic acid fragments are referred to as "transgenic" organisms. Examples of methods of plant transformation include *Agrobacterium*-mediated transformation (De Blaere et al. (1987) *Meth. Enzymol. 143*:277) and particle-accelerated or "gene gun" transformation technology (Klein et al. (1987) *Nature (London) 327*:70-73; U.S. Patent No. 4,945,050, incorporated herein by reference).

Standard recombinant DNA and molecular cloning techniques used herein are well known in the art and are described more fully in Sambrook et al. *Molecular Cloning: A Laboratory Manual*; Cold Spring Harbor Laboratory Press: Cold Spring Harbor, 1989 (hereinafter "Maniatis").

Nucleic acid fragments encoding at least a portion of a cellulose synthase enzyme have been isolated and identified by comparison of random plant cDNA sequences to public databases containing nucleotide and protein sequences using the BLAST algorithms well known to those skilled in the art. The nucleic acid fragments of the instant invention may be used to isolate cDNAs and genes encoding homologous proteins from the same or other plant species. Isolation of homologous genes using sequence-dependent protocols is well known in the art. Examples of sequence-dependent protocols include, but are not limited to, methods of nucleic acid hybridization, and methods of DNA and RNA amplification as exemplified by various uses of nucleic acid amplification technologies (e.g., polymerase chain reaction, ligase chain reaction).

For example, genes encoding other cellulose synthase enzymes, either as cDNAs or genomic DNAs, could be isolated directly by using all or a portion of the instant nucleic acid fragments as DNA hybridization probes to screen libraries from any desired plant employing

methodology well known to those skilled in the art. Specific oligonucleotide probes based upon the instant nucleic acid sequences can be designed and synthesized by methods known in the art (Maniatis). Moreover, the entire sequences can be used directly to synthesize DNA probes by methods known to the skilled artisan such as random primer DNA labeling, nick translation, or end-labeling techniques, or RNA probes using available *in vitro* transcription systems. In addition, specific primers can be designed and used to amplify a part or all of the instant sequences. The resulting amplification products can be labeled directly during amplification reactions or labeled after amplification reactions, and used as probes to isolate full length cDNA or genomic fragments under conditions of appropriate stringency.

In addition, two short segments of the instant nucleic acid fragments may be used in polymerase chain reaction protocols to amplify longer nucleic acid fragments encoding homologous genes from DNA or RNA. The polymerase chain reaction may also be performed on a library of cloned nucleic acid fragments wherein the sequence of one primer is derived from the instant nucleic acid fragments, and the sequence of the other primer takes advantage of the presence of the polyadenylic acid tracts to the 3' end of the mRNA precursor encoding plant genes. Alternatively, the second primer sequence may be based upon sequences derived from the cloning vector. For example, the skilled artisan can follow the RACE protocol (Frohman et al. (1988) *Proc. Natl. Acad. Sci. USA 85*:8998) to generate cDNAs by using PCR to amplify copies of the region between a single point in the transcript and the 3' or 5' end. Primers oriented in the 3' and 5' directions can be designed from the instant sequences. Using commercially available 3' RACE or 5' RACE systems (BRL), specific 3' or 5' cDNA fragments can be isolated (Ohara et al. (1989) *Proc. Natl. Acad. Sci. USA 86*:5673; Loh et al. (1989) *Science 243*:217). Products generated by the 3' and 5' RACE procedures can be combined to generate full-length cDNAs (Frohman and Martin (1989) *Techniques 1*:165).

Availability of the instant nucleotide and deduced amino acid sequences facilitates immunological screening of cDNA expression libraries. Synthetic peptides representing portions of the instant amino acid sequences may be synthesized. These peptides can be used to immunize animals to produce polyclonal or monoclonal antibodies with specificity for peptides or proteins comprising the amino acid sequences. These antibodies can be then be used to screen cDNA expression libraries to isolate full-length cDNA clones of interest (Lerner (1984) *Adv. Immunol. 36*:1; Maniatis).

The nucleic acid fragments of the instant invention may be used to create transgenic plants in which the disclosed polypeptides are present at higher or lower levels than normal or in cell types or developmental stages in which they are not normally found. This would have the effect of altering the level of cellulose synthase in those cells.

Overexpression of the proteins of the instant invention may be accomplished by first constructing a chimeric gene in which the coding region is operably linked to a promoter capable of directing expression of a gene in the desired tissues at the desired stage of development. For reasons of convenience, the chimeric gene may comprise promoter sequences and translation leader sequences derived from the same genes. 3' Non-coding sequences encoding transcription termination signals may also be provided. The instant chimeric gene may also comprise one or more introns in order to facilitate gene expression.

Plasmid vectors comprising the instant chimeric gene can then constructed. The choice of plasmid vector is dependent upon the method that will be used to transform host plants. The skilled artisan is well aware of the genetic elements that must be present on the plasmid vector in order to successfully transform, select and propagate host cells containing the chimeric gene. The skilled artisan will also recognize that different independent transformation events will result in different levels and patterns of expression (Jones et al. (1985) *EMBO J. 4*:2411-2418; De Almeida et al. (1989) *Mol. Gen. Genetics 218*:78-86), and thus that multiple events must be screened in order to obtain lines displaying the desired expression level and pattern. Such screening may be accomplished by Southern analysis of DNA, Northern analysis of mRNA expression, Western analysis of protein expression, or phenotypic analysis.

For some applications it may be useful to direct the instant polypeptides to different cellular compartments, or to facilitate its secretion from the cell. It is thus envisioned that the chimeric gene described above may be further supplemented by altering the coding sequence to encode the instant polypeptides with appropriate intracellular targeting sequences such as transit sequences (Keegstra (1989) *Cell 56*:247-253), signal sequences or sequences encoding endoplasmic reticulum localization (Chrispeels (1991) *Ann. Rev. Plant Phys. Plant Mol. Biol. 42*:21-53), or nuclear localization signals (Raikhel (1992) *Plant Phys.100*:1627-1632) added and/or with targeting sequences that are already present removed. While the references cited give examples of each of these, the list is not exhaustive and more targeting signals of utility may be discovered in the future.

It may also be desirable to reduce or eliminate expression of genes encoding the instant polypeptides in plants for some applications. In order to accomplish this, a chimeric gene designed for co-suppression of the instant polypeptide can be constructed by linking a gene or gene fragment encoding that polypeptide to plant promoter sequences. Alternatively, a chimeric gene designed to express antisense RNA for all or part of the instant nucleic acid fragment can be constructed by linking the gene or gene fragment in reverse orientation to plant promoter sequences. Either the co-suppression or antisense chimeric genes could be introduced into plants via transformation wherein expression of the corresponding endogenous genes are reduced or eliminated.

Molecular genetic solutions to the generation of plants with altered gene expression have a decided advantage over more traditional plant breeding approaches. Changes in plant phenotypes can be produced by specifically inhibiting expression of one or more genes by antisense inhibition or cosuppression (U. S. Patent Nos. 5,190,931, 5,107,065 and 5,283,323). An antisense or cosuppression construct would act as a dominant negative regulator of gene activity. While conventional mutations can yield negative regulation of gene activity these effects are most likely recessive. The dominant negative regulation available with a transgenic approach may be advantageous from a breeding perspective. In addition, the ability to restrict the expression of specific phenotype to the reproductive tissues of the plant by the use of tissue specific promoters may confer agronomic advantages relative to conventional mutations which may have an effect in all tissues in which a mutant gene is ordinarily expressed.

The person skilled in the art will know that special considerations are associated with the use of antisense or cosuppresion technologies in order to reduce expression of particular genes. For example, the proper level of expression of sense or antisense genes may require the use of different chimeric genes utilizing different regulatory elements known to the skilled artisan. Once transgenic plants are obtained by one of the methods described above, it will be necessary to screen individual transgenics for those that most effectively display the desired phenotype. Accordingly, the skilled artisan will develop methods for screening large numbers of transformants. The nature of these screens will generally be chosen on practical grounds, and is not an inherent part of the invention. For example, one can screen by looking for changes in gene expression by using antibodies specific for the protein encoded by the gene being suppressed, or one could establish assays that specifically measure enzyme activity. A preferred method will be one which allows large numbers of samples to be processed rapidly, since it will be expected that a large number of transformants will be negative for the desired phenotype.

The instant polypeptides (or portions thereof) may be produced in heterologous host cells, particularly in the cells of microbial hosts, and can be used to prepare antibodies to the these proteins by methods well known to those skilled in the art. The antibodies are useful for detecting the polypeptides of the instant invention *in situ* in cells or *in vitro* in cell extracts. Preferred heterologous host cells for production of the instant polypeptides are microbial hosts. Microbial expression systems and expression vectors containing regulatory sequences that direct high level expression of foreign proteins are well known to those skilled in the art. Any of these could be used to construct a chimeric gene for production of the instant polypeptides. This chimeric gene could then be introduced into appropriate microorganisms via transformation to provide high level expression of the encoded cellulose synthase. An example of a vector for high level expression of the instant polypeptides in a bacterial host is provided (Example 6).

Additionally, the instant polypeptides can be used as a targets to facilitate design and/or identification of inhibitors of those enzymes that may be useful as herbicides. This is desirable because the polypeptides described herein catalyze a step in the synthesis of cellulose. Accordingly, inhibition of the activity of one or more of the enzymes described herein could lead to inhibition plant growth. Thus, the instant polypeptides could be appropriate for new herbicide discovery and design.

All or a substantial portion of the nucleic acid fragments of the instant invention may also be used as probes for genetically and physically mapping the genes that they are a part of, and as markers for traits linked to those genes. Such information may be useful in plant breeding in order to develop lines with desired phenotypes. For example, the instant nucleic acid fragments may be used as restriction fragment length polymorphism (RFLP) markers. Southern blots (Maniatis) of restriction-digested plant genomic DNA may be probed with the nucleic acid fragments of the instant invention. The resulting banding patterns may then be subjected to genetic analyses using computer programs such as MapMaker (Lander et al. (1987) *Genomics 1*:174-181) in order to construct a genetic map. In addition, the nucleic acid fragments of the instant invention may be used to probe Southern blots containing restriction endonuclease-treated genomic DNAs of a set of individuals representing parent and progeny of a defined genetic cross. Segregation of the DNA polymorphisms is noted and used to calculate the position of the instant nucleic acid sequence in the genetic map previously obtained using this population (Botstein et al. (1980) *Am. J. Hum. Genet. 32*:314-331).

The production and use of plant gene-derived probes for use in genetic mapping is described in Bernatzky and Tanksley (1986) *Plant Mol. Biol. Reporter 4(1)*:37-41. Numerous publications describe genetic mapping of specific cDNA clones using the methodology outlined above or variations thereof. For example, F2 intercross populations, backcross populations, randomly mated populations, near isogenic lines, and other sets of individuals may be used for mapping. Such methodologies are well known to those skilled in the art.

Nucleic acid probes derived from the instant nucleic acid sequences may also be used for physical mapping (i.e., placement of sequences on physical maps; *see* Hoheisel et al. In: *Nonmammalian Genomic Analysis: A Practical Guide*, Academic press 1996, pp. 319-346, and references cited therein).

In another embodiment, nucleic acid probes derived from the instant nucleic acid sequences may be used in direct fluorescence *in situ* hybridization (FISH) mapping (Trask (1991) *Trends Genet. 7*:149-154). Although current methods of FISH mapping favor use of large clones (several to several hundred KB; see Laan et al. (1995) *Genome Research 5*:13-20), improvements in sensitivity may allow performance of FISH mapping using shorter probes.

A variety of nucleic acid amplification-based methods of genetic and physical mapping may be carried out using the instant nucleic acid sequences. Examples include allele-specific amplification (Kazazian (1989) *J. Lab. Clin. Med. 114(2)*:95-96), polymorphism of PCR-amplified fragments (CAPS; Sheffield et al. (1993) *Genomics 16*:325-332), allele-specific ligation (Landegren et al. (1988) *Science 241*:1077-1080), nucleotide extension reactions (Sokolov (1990) *Nucleic Acid Res. 18*:3671), Radiation Hybrid Mapping (Walter et al. (1997) *Nature Genetics 7*:22-28) and Happy Mapping (Dear and Cook (1989) *Nucleic Acid Res. 17*:6795-6807). For these methods, the sequence of a nucleic acid fragment is used to design and produce primer pairs for use in the amplification reaction or in primer extension reactions. The design of such primers is well known to those skilled in the art. In methods employing PCR-based genetic mapping, it may be necessary to identify DNA sequence differences between the parents of the mapping cross in the region corresponding to the instant nucleic acid sequence. This, however, is generally not necessary for mapping methods.

Loss of function mutant phenotypes may be identified for the instant cDNA clones either by targeted gene disruption protocols or by identifying specific mutants for these genes contained in a maize population carrying mutations in all possible genes (Ballinger and Benzer (1989) *Proc. Natl. Acad. Sci USA 86*:9402; Koes et al. (1995) *Proc. Natl. Acad. Sci USA 92*:8149; Bensen et al. (1995) *Plant Cell 7*:75). The latter approach may be accomplished in two ways. First, short segments of the instant nucleic acid fragments may be used in polymerase chain reaction protocols in conjunction with a mutation tag sequence primer on DNAs prepared from a population of plants in which Mutator transposons or some other mutation-causing DNA element has been introduced (see Bensen, *supra*). The amplification of a specific DNA fragment with these primers indicates the insertion of the mutation tag element in or near the plant gene encoding the instant polypeptides. Alternatively, the instant nucleic acid fragment may be used as a hybridization probe against PCR amplification products generated from the mutation population using the mutation tag sequence primer in conjunction with an arbitrary genomic site primer, such as that for a restriction enzyme site-anchored synthetic adaptor. With either method, a plant containing a mutation in the endogenous gene encoding the instant polypeptides can be identified and obtained. This mutant plant can then be used to determine or confirm the natural function of the instant polypeptides disclosed herein.

EXAMPLES

The present invention is further defined in the following Examples, in which all parts and percentages are by weight and degrees are Celsius, unless otherwise stated. It should be understood that these Examples, while indicating preferred embodiments of the invention, are given by way of illustration only. From the above discussion and these Examples, one skilled in the art can ascertain the essential characteristics of this invention, and without

departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions.

EXAMPLE 1

Composition of cDNA Libraries; Isolation and Sequencing of cDNA Clones

cDNA libraries representing mRNAs from various barley, corn, rice, soybean and wheat tissues were prepared. The characteristics of the libraries are described below.

TABLE 2

cDNA Libraries from Barley, Corn, Rice, Soybean and Wheat

Library	Tissue	Clone
bsh1	Barley (*Hordeum vulgare*) sheath, developing seedling	bsh1.pk0002.f6
cco1n	Corn (*Zea mays*) cob of 67 day old plants grown in green house*	cco1n.pk0005.g3
cdt2c	Corn (*Zea mays*) developing tassel 2	cdt2c.pk002.g1
		cdt2c.pk002.l16
cr1n	Corn (*Zea mays*) root from 7 day seedlings grown in light*	cr1n.pk0135.e10
csc1c	Corn (*Zea mays*) 20 day seedling (germination under cold stress)	csc1c.pk002.i1
p0031	Corn (*Zea mays*) shoot culture, initiated from seed derived meristems culture was maintained on 273N medium.	p0031.ccmar05rb
p0110	Corn (*Zea mays*) stages V3/V4** leaf tissue minus midrib harvested 4 hours, 24 hours and 7 days after infiltration with salicylic acid, tissues pooled*	p0110.cgsma57r
p0097	Corn (*Zea mays*) stage V9** whorl section (7 cm) from plant infected four times with european corn borer	p0097.cqrad17rc
p0122	Corn (*Zea mays*) pith tissue collected from internode subtending ear node 5 days after pollenation	p0122.ckamh70rc
rlr24	Rice (*Oryza sativa*) leaf (15 days after germination) 24 hours after infection of *Magaporthe grisea* strain 4360-R-62 (AVR2-YAMO); Resistant	rlr24.pk0073.g1
sdp2c	Soybean (*Glycine max*) developing pods 6-7 mm	sdp2c.pk005.o22
ses8w	Soybean (*Glycine max*) mature embryo 8 weeks after subculture	ses8w.pk0028.f3
ss1	Soybean (*Glycine max*) seedling 5-10 day	ssl.pk0036.c10
wl1	Wheat (*Triticum aestivum*) leaf 7 day old seedling, light grown	wl1.pk0009.c9
wl1n	Wheat (*Triticum aestivum*) leaf 7 day old seedling, light grown*	wl1n.pk0044.b1
wr1	Wheat (*Triticum aestivum*) root; 7 day old seedling, light grown	wr1.pk0160.d11

Library	Tissue	Clone
wre1n	Wheat (*Triticum aestivum*) root; 7 day old etiolated seedling*	wre1n.pk0043.f9
		wre1n.pk0043.h8
		wre1n.pk0131.g10

*These libraries were normalized essentially as described in U.S. Patent No. 5,482,845, incorporated herein by reference.

**V3, V4 and V9 refer to stages of corn growth. The descriptions can be found in "How a Corn Plant Develops" Special Report No. 48, Iowa State University of Science and Technology Cooperative Extension Service Ames,Iowa, Reprinted February 1993.

cDNA libraries may be prepared by any one of many methods available. For example, the cDNAs may be introduced into plasmid vectors by first preparing the cDNA libraries in Uni-ZAP™ XR vectors according to the manufacturer's protocol (Stratagene Cloning Systems, La Jolla, CA). The Uni-ZAP™ XR libraries are converted into plasmid libraries according to the protocol provided by Stratagene. Upon conversion, cDNA inserts will be contained in the plasmid vector pBluescript. In addition, the cDNAs may be introduced directly into precut Bluescript II SK(+) vectors (Stratagene) using T4 DNA ligase (New England Biolabs), followed by transfection into DH10B cells according to the manufacturer's protocol (GIBCO BRL Products). Once the cDNA inserts are in plasmid vectors, plasmid DNAs are prepared from randomly picked bacterial colonies containing recombinant pBluescript plasmids, or the insert cDNA sequences are amplified via polymerase chain reaction using primers specific for vector sequences flanking the inserted cDNA sequences. Amplified insert DNAs or plasmid DNAs are sequenced in dye-primer sequencing reactions to generate partial cDNA sequences (expressed sequence tags or "ESTs"; see Adams et al., (1991) *Science 252*:1651). The resulting ESTs are analyzed using a Perkin Elmer Model 377 fluorescent sequencer.

EXAMPLE 2

Identification of cDNA Clones

cDNA clones encoding cellulose synthase enzymes were identified by conducting BLAST (Basic Local Alignment Search Tool; Altschul et al. (1993) *J. Mol. Biol. 215*:403-410; see also www.ncbi.nlm.nih.gov/BLAST/) searches for similarity to sequences contained in the BLAST "nr" database (comprising all non-redundant GenBank CDS translations, sequences derived from the 3-dimensional structure Brookhaven Protein Data Bank, the last major release of the SWISS-PROT protein sequence database, EMBL, and DDBJ databases). The cDNA sequences obtained in Example 1 were analyzed for similarity to all publicly available DNA sequences contained in the "nr" database using the BLASTN algorithm provided by the National Center for Biotechnology Information (NCBI). The

DNA sequences were translated in all reading frames and compared for similarity to all publicly available protein sequences contained in the "nr" database using the BLASTX algorithm (Gish and States (1993) *Nature Genetics 3*:266-272) provided by the NCBI. For convenience, the P-value (probability) of observing a match of a cDNA sequence to a sequence contained in the searched databases merely by chance as calculated by BLAST are reported herein as "pLog" values, which represent the negative of the logarithm of the reported P-value. Accordingly, the greater the pLog value, the greater the likelihood that the cDNA sequence and the BLAST "hit" represent homologous proteins.

EXAMPLE 3

Characterization of cDNA Clones Encoding Cellulose Synthase

The BLASTX search using the EST sequences from clones listed in Table 3 revealed similarity of the polypeptides encoded by the cDNAs to cellulose synthase from *Arabidopsis thaliana* (NCBI Identifier No. gi 2827139, gi 2827141, gi 4467125, gi 4886756 and gi 3135611) and *Gossypium hirsutum* (NCBI Identifier No. gi 1706958 and 5081779). Shown in Table 3 are the BLAST results for individual ESTs ("EST"), the sequences of the entire cDNA inserts comprising the indicated cDNA clones ("FIS"), complete gene sequences ("CGS") or contigs assembled from two or more ESTs ("Contig"):

TABLE 3

BLAST Results for Sequences Encoding Polypeptides Homologous to *Arabidopsis thaliana* and *Gossypium hirsutum* Cellulose Synthase

Clone	Status	BLAST pLog Score
bsh1.pk0002.f6	FIS	154.00 (gi 2827139)
Contig composed of: cco1n.pk0005.g3 cdt2c.pk002.g1 cdt2c.pk002.l16 csc1c.pk002.i1 p0031.ccmar05rb p0110.cgsma57r	Contig	>254.00 (gi 2827141)
cr1n.pk0135.e10	FIS	176.00 (gi 1706958)
p0097.cqrad17rc	CGS	>254.00 (gi 2827141)
p0122.ckamh70rc	CGS	>254.00 (gi 2827141)
rlr24.pk0073.g1	EST	77.70 (gi 4467125)
sdp2c.pk005.o22	FIS	>254.00 (gi 4886756)
ses8w.pk0028.f3	EST	>254.00 (gi 2827139)
ssl.pk0036.c10	EST	>254.00 (gi 2827141)
Contig composed of: wl1.pk0009.c9 wr1.pk0160.d11 wre1n.pk0043.f9	Contig	>254.00 (gi 5081779)

wre1n.pk0043.h8 wre1n.pk0131.g10		
wl1n.pk0044.b1	EST	166.00 (gi 3135611)

Figure 1 presents an alignment of the amino acid sequences set forth in SEQ ID NOs:2, 4, 8, 10, 12, 14, 16, 18, 20 and 22 and the *Arabidopsis thaliana* (SEQ ID NOs:23 (gi 2827139), 24 (gi 2827141), 26 (gi 4467125), 27 (gi 4886756) and 29 (gi 3135611)) and *Gossypium hirsutum* (SEQ ID NOs:25 (gi 1706958) and 28 (gi 5081779)) sequences. The data in Table 4 represents a calculation of the percent identity of the amino acid sequences set forth in SEQ ID NOs:2, 4, 8, 10, 12, 14, 16, 18, 20 and 22 and the *Arabidopsis thaliana* (SEQ ID NOs:23, 24, 26, 27 and 29) and *Gossypium hirsutum* (SEQ ID NOs:25 and 28) sequences.

TABLE 4

Percent Identity of Amino Acid Sequences Deduced From the Nucleotide Sequences of cDNA Clones Encoding Polypeptides Homologous to *Arabidopsis thaliana* and *Gossypium hirsutum* Cellulose Synthase

SEQ ID NO.	Percent Identity to
2	82% (gi 2827139)
4	69% (gi 2827141)
6	89% (gi 1706958)
8	70% (gi 2827141)
10	70% (gi 2827141)
12	36% (gi 4467125)
14	86% (gi 4886756)
16	88% (gi 2827139)
18	86% (gi 2827141)
20	87% (gi 5081779)
22	70% (gi 3135611)

Sequence alignments and percent identity calculations were performed using the Megalign program of the LASARGENE bioinformatics computing suite (DNASTAR Inc., Madison, WI). Multiple alignment of the sequences was performed using the Clustal method of alignment (Higgins and Sharp (1989) *CABIOS.* *5*:151-153) with the default parameters (GAP PENALTY=10, GAP LENGTH PENALTY=10). Default parameters for pairwise alignments using the Clustal method were KTUPLE 1, GAP PENALTY=3, WINDOW=5 and DIAGONALS SAVED=5. Sequence alignments and BLAST scores and probabilities indicate that the nucleic acid fragments comprising the instant cDNA clones

encode a substantial portion of a cellulose synthase. These sequences represent the first barley, corn, rice, soybean and wheat sequences encoding cellulose synthase.

EXAMPLE 4

Expression of Chimeric Genes in Monocot Cells

A chimeric gene comprising a cDNA encoding the instant polypeptides in sense orientation with respect to the maize 27 kD zein promoter that is located 5' to the cDNA fragment, and the 10 kD zein 3' end that is located 3' to the cDNA fragment, can be constructed. The cDNA fragment of this gene may be generated by polymerase chain reaction (PCR) of the cDNA clone using appropriate oligonucleotide primers. Cloning sites (NcoI or SmaI) can be incorporated into the oligonucleotides to provide proper orientation of the DNA fragment when inserted into the digested vector pML103 as described below. Amplification is then performed in a standard PCR. The amplified DNA is then digested with restriction enzymes NcoI and SmaI and fractionated on an agarose gel. The appropriate band can be isolated from the gel and combined with a 4.9 kb NcoI-SmaI fragment of the plasmid pML103. Plasmid pML103 has been deposited under the terms of the Budapest Treaty at ATCC (American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209), and bears accession number ATCC 97366. The DNA segment from pML103 contains a 1.05 kb SalI-NcoI promoter fragment of the maize 27 kD zein gene and a 0.96 kb SmaI-SalI fragment from the 3' end of the maize 10 kD zein gene in the vector pGem9Zf(+) (Promega). Vector and insert DNA can be ligated at 15°C overnight, essentially as described (Maniatis). The ligated DNA may then be used to transform *E. coli* XL1-Blue (Epicurian Coli XL-1 Blue™; Stratagene). Bacterial transformants can be screened by restriction enzyme digestion of plasmid DNA and limited nucleotide sequence analysis using the dideoxy chain termination method (Sequenase™ DNA Sequencing Kit; U.S. Biochemical). The resulting plasmid construct would comprise a chimeric gene encoding, in the 5' to 3' direction, the maize 27 kD zein promoter, a cDNA fragment encoding the instant polypeptides, and the 10 kD zein 3' region.

The chimeric gene described above can then be introduced into corn cells by the following procedure. Immature corn embryos can be dissected from developing caryopses derived from crosses of the inbred corn lines H99 and LH132. The embryos are isolated 10 to 11 days after pollination when they are 1.0 to 1.5 mm long. The embryos are then placed with the axis-side facing down and in contact with agarose-solidified N6 medium (Chu et al. (1975) *Sci. Sin. Peking* 18:659-668). The embryos are kept in the dark at 27°C. Friable embryogenic callus consisting of undifferentiated masses of cells with somatic proembryoids and embryoids borne on suspensor structures proliferates from the scutellum of these immature embryos. The embryogenic callus isolated from the primary explant can be cultured on N6 medium and sub-cultured on this medium every 2 to 3 weeks.

The plasmid, p35S/Ac (obtained from Dr. Peter Eckes, Hoechst Ag, Frankfurt, Germany) may be used in transformation experiments in order to provide for a selectable marker. This plasmid contains the *Pat* gene (see European Patent Publication 0 242 236) which encodes phosphinothricin acetyl transferase (PAT). The enzyme PAT confers resistance to herbicidal glutamine synthetase inhibitors such as phosphinothricin. The *pat* gene in p35S/Ac is under the control of the 35S promoter from Cauliflower Mosaic Virus (Odell et al. (1985) *Nature* 313:810-812) and the 3' region of the nopaline synthase gene from the T-DNA of the Ti plasmid of *Agrobacterium tumefaciens*.

The particle bombardment method (Klein et al. (1987) *Nature* 327:70-73) may be used to transfer genes to the callus culture cells. According to this method, gold particles (1 μm in diameter) are coated with DNA using the following technique. Ten μg of plasmid DNAs are added to 50 μL of a suspension of gold particles (60 mg per mL). Calcium chloride (50 μL of a 2.5 M solution) and spermidine free base (20 μL of a 1.0 M solution) are added to the particles. The suspension is vortexed during the addition of these solutions. After 10 minutes, the tubes are briefly centrifuged (5 sec at 15,000 rpm) and the supernatant removed. The particles are resuspended in 200 μL of absolute ethanol, centrifuged again and the supernatant removed. The ethanol rinse is performed again and the particles resuspended in a final volume of 30 μL of ethanol. An aliquot (5 μL) of the DNA-coated gold particles can be placed in the center of a Kapton™ flying disc (Bio-Rad Labs). The particles are then accelerated into the corn tissue with a Biolistic™ PDS-1000/He (Bio-Rad Instruments, Hercules CA), using a helium pressure of 1000 psi, a gap distance of 0.5 cm and a flying distance of 1.0 cm.

For bombardment, the embryogenic tissue is placed on filter paper over agarose-solidified N6 medium. The tissue is arranged as a thin lawn and covered a circular area of about 5 cm in diameter. The petri dish containing the tissue can be placed in the chamber of the PDS-1000/He approximately 8 cm from the stopping screen. The air in the chamber is then evacuated to a vacuum of 28 inches of Hg. The macrocarrier is accelerated with a helium shock wave using a rupture membrane that bursts when the He pressure in the shock tube reaches 1000 psi.

Seven days after bombardment the tissue can be transferred to N6 medium that contains gluphosinate (2 mg per liter) and lacks casein or proline. The tissue continues to grow slowly on this medium. After an additional 2 weeks the tissue can be transferred to fresh N6 medium containing gluphosinate. After 6 weeks, areas of about 1 cm in diameter of actively growing callus can be identified on some of the plates containing the glufosinate-supplemented medium. These calli may continue to grow when sub-cultured on the selective medium.

Plants can be regenerated from the transgenic callus by first transferring clusters of tissue to N6 medium supplemented with 0.2 mg per liter of 2,4-D. After two weeks the

tissue can be transferred to regeneration medium (Fromm et al. (1990) *Bio/Technology* *8*:833-839).

EXAMPLE 5

Expression of Chimeric Genes in Dicot Cells

A seed-specific expression cassette composed of the promoter and transcription terminator from the gene encoding the β subunit of the seed storage protein phaseolin from the bean *Phaseolus vulgaris* (Doyle et al. (1986) *J. Biol. Chem. 261*:9228-9238) can be used for expression of the instant polypeptides in transformed soybean. The phaseolin cassette includes about 500 nucleotides upstream (5') from the translation initiation codon and about 1650 nucleotides downstream (3') from the translation stop codon of phaseolin. Between the 5' and 3' regions are the unique restriction endonuclease sites Nco I (which includes the ATG translation initiation codon), Sma I, Kpn I and Xba I. The entire cassette is flanked by Hind III sites.

The cDNA fragment of this gene may be generated by polymerase chain reaction (PCR) of the cDNA clone using appropriate oligonucleotide primers. Cloning sites can be incorporated into the oligonucleotides to provide proper orientation of the DNA fragment when inserted into the expression vector. Amplification is then performed as described above, and the isolated fragment is inserted into a pUC18 vector carrying the seed expression cassette.

Soybean embroys may then be transformed with the expression vector comprising sequences encoding the instant polypeptides. To induce somatic embryos, cotyledons, 3-5 mm in length dissected from surface sterilized, immature seeds of the soybean cultivar A2872, can be cultured in the light or dark at 26°C on an appropriate agar medium for 6-10 weeks. Somatic embryos which produce secondary embryos are then excised and placed into a suitable liquid medium. After repeated selection for clusters of somatic embryos which multiplied as early, globular staged embryos, the suspensions are maintained as described below.

Soybean embryogenic suspension cultures can maintained in 35 mL liquid media on a rotary shaker, 150 rpm, at 26°C with florescent lights on a 16:8 hour day/night schedule. Cultures are subcultured every two weeks by inoculating approximately 35 mg of tissue into 35 mL of liquid medium.

Soybean embryogenic suspension cultures may then be transformed by the method of particle gun bombardment (Klein et al. (1987) *Nature* (London) *327*:70, U.S. Patent No. 4,945,050). A DuPont Biolistic™ PDS1000/HE instrument (helium retrofit) can be used for these transformations.

A selectable marker gene which can be used to facilitate soybean transformation is a chimeric gene composed of the 35S promoter from Cauliflower Mosaic Virus (Odell et al. (1985) *Nature 313*:810-812), the hygromycin phosphotransferase gene from plasmid pJR225

(from *E. coli*; Gritz et al.(1983) *Gene 25*:179-188) and the 3' region of the nopaline synthase gene from the T-DNA of the Ti plasmid of *Agrobacterium tumefaciens*. The seed expression cassette comprising the phaseolin 5' region, the fragment encoding the instant polypeptides and the phaseolin 3' region can be isolated as a restriction fragment. This fragment can then be inserted into a unique restriction site of the vector carrying the marker gene.

To 50 µL of a 60 mg/mL 1 µm gold particle suspension is added (in order): 5 µL DNA (1 µg/µL), 20 µl spermidine (0.1 M), and 50 µL $CaCl_2$ (2.5 M). The particle preparation is then agitated for three minutes, spun in a microfuge for 10 seconds and the supernatant removed. The DNA-coated particles are then washed once in 400 µL 70% ethanol and resuspended in 40 µL of anhydrous ethanol. The DNA/particle suspension can be sonicated three times for one second each. Five µL of the DNA-coated gold particles are then loaded on each macro carrier disk.

Approximately 300-400 mg of a two-week-old suspension culture is placed in an empty 60x15 mm petri dish and the residual liquid removed from the tissue with a pipette. For each transformation experiment, approximately 5-10 plates of tissue are normally bombarded. Membrane rupture pressure is set at 1100 psi and the chamber is evacuated to a vacuum of 28 inches mercury. The tissue is placed approximately 3.5 inches away from the retaining screen and bombarded three times. Following bombardment, the tissue can be divided in half and placed back into liquid and cultured as described above.

Five to seven days post bombardment, the liquid media may be exchanged with fresh media, and eleven to twelve days post bombardment with fresh media containing 50 mg/mL hygromycin. This selective media can be refreshed weekly. Seven to eight weeks post bombardment, green, transformed tissue may be observed growing from untransformed, necrotic embryogenic clusters. Isolated green tissue is removed and inoculated into individual flasks to generate new, clonally propagated, transformed embryogenic suspension cultures. Each new line may be treated as an independent transformation event. These suspensions can then be subcultured and maintained as clusters of immature embryos or regenerated into whole plants by maturation and germination of individual somatic embryos.

EXAMPLE 6

Expression of Chimeric Genes in Microbial Cells

The cDNAs encoding the instant polypeptides can be inserted into the T7 *E. coli* expression vector pBT430. This vector is a derivative of pET-3a (Rosenberg et al. (1987) *Gene 56*:125-135) which employs the bacteriophage T7 RNA polymerase/T7 promoter system. Plasmid pBT430 was constructed by first destroying the EcoR I and Hind III sites in pET-3a at their original positions. An oligonucleotide adaptor containing EcoR I and Hind III sites was inserted at the BamH I site of pET-3a. This created pET-3aM with additional unique cloning sites for insertion of genes into the expression vector. Then, the Nde I site at the position of translation initiation was converted to an Nco I site using

oligonucleotide-directed mutagenesis. The DNA sequence of pET-3aM in this region, 5'-CATATGG, was converted to 5'-CCCATGG in pBT430.

Plasmid DNA containing a cDNA may be appropriately digested to release a nucleic acid fragment encoding the protein. This fragment may then be purified on a 1% NuSieve GTG™ low melting agarose gel (FMC). Buffer and agarose contain 10 μg/ml ethidium bromide for visualization of the DNA fragment. The fragment can then be purified from the agarose gel by digestion with GELase™ (Epicentre Technologies) according to the manufacturer's instructions, ethanol precipitated, dried and resuspended in 20 μL of water. Appropriate oligonucleotide adapters may be ligated to the fragment using T4 DNA ligase (New England Biolabs, Beverly, MA). The fragment containing the ligated adapters can be purified from the excess adapters using low melting agarose as described above. The vector pBT430 is digested, dephosphorylated with alkaline phosphatase (NEB) and deproteinized with phenol/chloroform as described above. The prepared vector pBT430 and fragment can then be ligated at 16°C for 15 hours followed by transformation into DH5 electrocompetent cells (GIBCO BRL). Transformants can be selected on agar plates containing LB media and 100 μg/mL ampicillin. Transformants containing the gene encoding the instant polypeptides are then screened for the correct orientation with respect to the T7 promoter by restriction enzyme analysis.

For high level expression, a plasmid clone with the cDNA insert in the correct orientation relative to the T7 promoter can be transformed into *E. coli* strain BL21(DE3) (Studier et al. (1986) *J. Mol. Biol. 189*:113-130). Cultures are grown in LB medium containing ampicillin (100 mg/L) at 25°C. At an optical density at 600 nm of approximately 1, IPTG (isopropylthio-β-galactoside, the inducer) can be added to a final concentration of 0.4 mM and incubation can be continued for 3 h at 25°. Cells are then harvested by centrifugation and re-suspended in 50 μL of 50 mM Tris-HCl at pH 8.0 containing 0.1 mM DTT and 0.2 mM phenyl methylsulfonyl fluoride. A small amount of 1 mm glass beads can be added and the mixture sonicated 3 times for about 5 seconds each time with a microprobe sonicator. The mixture is centrifuged and the protein concentration of the supernatant determined. One μg of protein from the soluble fraction of the culture can be separated by SDS-polyacrylamide gel electrophoresis. Gels can be observed for protein bands migrating at the expected molecular weight.

EXAMPLE 7

Evaluating Compounds for Their Ability to Inhibit the Activity of Cellulose Synthase

The polypeptides described herein may be produced using any number of methods known to those skilled in the art. Such methods include, but are not limited to, expression in bacteria as described in Example 6, or expression in eukaryotic cell culture, *in planta*, and using viral expression systems in suitably infected organisms or cell lines. The instant

polypeptides may be expressed either as mature forms of the proteins as observed *in vivo* or as fusion proteins by covalent attachment to a variety of enzymes, proteins or affinity tags. Common fusion protein partners include glutathione S-transferase ("GST"), thioredoxin ("Trx"), maltose binding protein, and C- and/or N-terminal hexahistidine polypeptide ("$(His)_6$"). The fusion proteins may be engineered with a protease recognition site at the fusion point so that fusion partners can be separated by protease digestion to yield intact mature enzyme. Examples of such proteases include thrombin, enterokinase and factor Xa. However, any protease can be used which specifically cleaves the peptide connecting the fusion protein and the enzyme.

Purification of the instant polypeptides, if desired, may utilize any number of separation technologies familiar to those skilled in the art of protein purification. Examples of such methods include, but are not limited to, homogenization, filtration, centrifugation, heat denaturation, ammonium sulfate precipitation, desalting, pH precipitation, ion exchange chromatography, hydrophobic interaction chromatography and affinity chromatography, wherein the affinity ligand represents a substrate, substrate analog or inhibitor. When the instant polypeptides are expressed as fusion proteins, the purification protocol may include the use of an affinity resin which is specific for the fusion protein tag attached to the expressed enzyme or an affinity resin containing ligands which are specific for the enzyme. For example, the instant polypeptides may be expressed as a fusion protein coupled to the C-terminus of thioredoxin. In addition, a $(His)_6$ peptide may be engineered into the N-terminus of the fused thioredoxin moiety to afford additional opportunities for affinity purification. Other suitable affinity resins could be synthesized by linking the appropriate ligands to any suitable resin such as Sepharose-4B. In an alternate embodiment, a thioredoxin fusion protein may be eluted using dithiothreitol; however, elution may be accomplished using other reagents which interact to displace the thioredoxin from the resin. These reagents include β–mercaptoethanol or other reduced thiol. The eluted fusion protein may be subjected to further purification by traditional means as stated above, if desired. Proteolytic cleavage of the thioredoxin fusion protein and the enzyme may be accomplished after the fusion protein is purified or while the protein is still bound to the ThioBond™ affinity resin or other resin.

Crude, partially purified or purified enzyme, either alone or as a fusion protein, may be utilized in assays for the evaluation of compounds for their ability to inhibit enzymatic activation of the instant polypeptides disclosed herein. Assays may be conducted under well known experimental conditions which permit optimal enzymatic activity. For example, assays for cellulose synthase activity are presented in WO 98/18949 and WO 98/00549.

CLAIMS

What is claimed is:

1. An isolated nucleic acid fragment comprising at least 900 nucleotides, wherein the nucleic acid fragment encodes a cellulose synthase comprising a member selected from the group consisting of:

(a) an isolated nucleic acid fragment encoding an amino acid sequence that is at least 90% identical to the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:2, 6, 12, 14, 16, 18, 20 and 22;

(b) an isolated nucleic acid fragment that is complementary to (a).

2. The isolated nucleic acid fragment of Claim 1 wherein nucleic acid fragment is a functional RNA.

3. The isolated nucleic acid fragment of Claim 1 wherein the nucleotide sequence of the fragment comprises the sequence set forth in a member selected from the group consisting of SEQ ID NO:1, 5, 11, 13, 15, 17, 19 and 21.

4. A chimeric gene comprising the nucleic acid fragment of Claim 1 operably linked to suitable regulatory sequences.

5. A transformed host cell comprising the chimeric gene of Claim 4.

6. A cellulose synthase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:2, 6, 12, 14, 16, 18, 20 and 22.

7. An isolated nucleic acid fragment encoding a cellulose synthase comprising a member selected from the group consisting of:

(a) an isolated nucleic acid fragment encoding an amino acid sequence that is functionally acitve polypeptide and at least 80% identical to the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:4, 8 and 10 ;

(b) an isolated nucleic acid fragment that is complementary to (a).

8. The isolated nucleic acid fragment of Claim 7 wherein nucleic acid fragment is a functional RNA.

9. The isolated nucleic acid fragment of Claim 7 wherein the nucleotide sequence of the fragment comprises the sequence set forth in a member selected from the group consisting of SEQ ID NO:3, 7 and 9.

10. A chimeric gene comprising the nucleic acid fragment of Claim 7 operably linked to suitable regulatory sequences.

11. A transformed host cell comprising the chimeric gene of Claim 10.

12. A cellulose synthase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:4, 8, 10.

13. A method of altering the level of expression of a cellulose synthase in a host cell comprising:

(a) transforming a host cell with the chimeric gene of any of Claims 4 and 10; and

(b) growing the transformed host cell produced in step (a) under conditions that are suitable for expression of the chimeric gene

wherein expression of the chimeric gene results in production of altered levels of a cellulose synthase in the transformed host cell.

14. A method of obtaining a nucleic acid fragment encoding all or a substantial portion of the amino acid sequence encoding a cellulose synthase comprising:

(a) probing a cDNA or genomic library with the nucleic acid fragment of any of Claims 1 and 7;

(b) identifying a DNA clone that hybridizes with the nucleic acid fragment any of of Claims 1and 7;

(c) isolating the DNA clone identified in step (b); and

(d) sequencing the cDNA or genomic fragment that comprises the clone isolated in step (c)

wherein the sequenced nucleic acid fragment encodes all or a substantial portion of the amino acid sequence encoding a cellulose synthase.

15. A method of obtaining a nucleic acid fragment encoding a substantial portion of an amino acid sequence encoding a cellulose synthase comprising:

(a) synthesizing an oligonucleotide primer corresponding to a portion of the sequence set forth in any of SEQ ID NOs:1, 3, 5, 7, 9, 11, 13, 15, 17, 19 and 21; and

(b) amplifying a cDNA insert present in a cloning vector using the oligonucleotide primer of step (a) and a primer representing sequences of the cloning vector

wherein the amplified nucleic acid fragment encodes a substantial portion of an amino acid sequence encoding a cellulose synthase.

16. The product of the method of Claim 14.

17. The product of the method of Claim 15.

18. A method for evaluating at least one compound for its ability to inhibit the activity of a cellulose synthase, the method comprising the steps of:

(a) transforming a host cell with a chimeric gene comprising a nucleic acid fragment encoding a cellulose synthase, operably linked to suitable regulatory sequences;

(b) growing the transformed host cell under conditions that are suitable for expression of the chimeric gene wherein expression of the chimeric gene results in production of the cellulose synthase encoded by the operably linked nucleic acid fragment in the transformed host cell;

(c) optionally purifying the cellulose synthase expressed by the transformed host cell;

(d) treating the cellulose synthase with a compound to be tested; and

(e) comparing the activity of the cellulose synthase that has been treated with a test compound to the activity of an untreated cellulose synthase,

thereby selecting compounds with potential for inhibitory activity.

Figure 1

```
             1                                                          60
SEQ ID NO:2  ------------------------------------------------------------
SEQ ID NO:4  RAAQAQRNKGKPQPEEQKLASVSLP--LPHSRFIPFPPRRRYRRR---RTHACPG----I
SEQ ID NO:6  ------------------------------------------------------------
SEQ ID NO:8  HSSYTKSRSSLAQPRAAPRQAQPPP--ATAACACERSPRPGDQRRGGLRAFRCAAAAGFV
SEQ ID NO:10 ------------------------------------------------------------
SEQ ID NO:12 RCS---RRWTCSSPPPTPTRSRRSPRRTP-------------------------------
SEQ ID NO:14 ------------------------------------------------------------
SEQ ID NO:16 ------------------------------------------------------------
SEQ ID NO:18 ------------------------------------------------------------
SEQ ID NO:20 ------------------------------------------------------------
SEQ ID NO:22 ------------------------------------------------------------
SEQ ID NO:23 ------------------------------------------------------------
SEQ ID NO:24 MNTGGR------------------------------------------------------
SEQ ID NO:25 ------------------------------------------------------------
SEQ ID NO:26 MASTPPQTSKKVRNNSGSGQTVKFARRTSSGRYVSLS-RDNIELSGELSGDYSNYTVHIP
SEQ ID NO:27 ------------------------------------------------------------
SEQ ID NO:28 ------------------------------------------------------------
SEQ ID NO:29 R---PR------------------------------------------------------

             61                                                        120
SEQ ID NO:2  ------------------------------------------------------------
SEQ ID NO:4  W-RSGSARG----ME-ASAGLVAGSHNRNELV-VIRRDGEPGPKP--MDQRNGQVCQI--
SEQ ID NO:6  ------------------------------------------------------------
SEQ ID NO:8  RERDPAGRGGGPEME-ASAGLVAGSHNRNELV-VIRRDRESGAAGGGAARRAEAPCQI--
SEQ ID NO:10 -------------ME-ASAGLVAGSHNRNELV-VIRRDGDPGPKP--PREQNGQVCQI--
SEQ ID NO:12 -------------------------------------------------------C----
SEQ ID NO:14 -------------ME-ASAGLVAGSHNRNELV-VIHGHEEP--KA--LKNLDGQVCEI--
SEQ ID NO:16 ------------------------------------------------------------
SEQ ID NO:18 ------------------------------------------------------------
SEQ ID NO:20 ------------------------------------------------------------
SEQ ID NO:22 ------------------------------------------------------------
SEQ ID NO:23 -------------ME-ASAGLVAGSYRRNELV-RIRHESDGGTKP--LKNMNGQICQI--
SEQ ID NO:24 --------------------LIAGSHNRNEFV-LI--NADESARIRSVQELSGQTCQI--
SEQ ID NO:25 ------------------------------------------------------------
SEQ ID NO:26 PTPDNQPMATKAEEQYVSNSLFTGGFNSVTRAHLMDKVIDSDVTHPQMAGAKGSSCAMPA
SEQ ID NO:27 -------------ME-ASAGLVAGSHNRNELV-VIHNHEEP--KP--LKNLDGQFCEI--
SEQ ID NO:28 ------------------------------------------------------------
SEQ ID NO:29 --------------------LIAGSHNRNEFV-LI--NADENARIRSVQELSGQTCQI--

             121                                                       180
SEQ ID NO:2  ------------------------------------------------------------
SEQ ID NO:4  CGDDVGRNPDGEPFVACNECAFPICRDCYEYERREGTQNCPQCKTRFKRLKGCARVPGD-
SEQ ID NO:6  ------------------------------------------------------------
SEQ ID NO:8  CGDEVGVGFDGEPFVACNECAFPVCRACYEYERREGSQACPQCRTRYKRLKGCPRVAGD-
SEQ ID NO:10 CGDDVGLAPGGDPFVACNECAFPVCRDCYEYERREGTQNCPQCKTRYKRLKGCQRVTGD-
SEQ ID NO:12 -------------------CPY--------------------------------------
SEQ ID NO:14 CGDGVGLTVDGDLFVACNECGFPVCRPCYEYERREGSHLCPQCKTRYKRLKGSPRVEGDD
SEQ ID NO:16 ------------------------------------------------------------
SEQ ID NO:18 ------------------------------------------------------------
SEQ ID NO:20 ------------------------------------------------------------
SEQ ID NO:22 ------------------------------------------------------------
SEQ ID NO:23 CGDDVGLAETGDVFVACNECAFPVCRPCYEYERKDGTQCCPQCKTRFRRHRGSPRVEGDE
SEQ ID NO:24 CGDEIELTVSSELFVACNECAFPVCRPCYEYERREGNQACPQCKTRYKRIKGSPRVDGDD
SEQ ID NO:25 ------------------------------------------------------------
SEQ ID NO:26 CDGNVMKDERGKDVMPC-ECRFKICRDCFMDAQKE-TGLCPGCKEQYK------------
```

Figure 1 (cont'd.)

```
SEQ ID NO:27  CGDQIGLTVEGDLFVACNECGFPACRPCYEYERREGTQNCPQCKTRYKRLRGSPRVEGDE
SEQ ID NO:28  ------------------------------------------------------------
SEQ ID NO:29  CRDEIELTVDGEPFVACNECAFPVCRPCYEYERREGNQACPQCKTRFKRLKGSPRVEGD-

              181                                                      240
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   EEEDGVDDLENEFNWSDK----HDSQYLAESMLHAHMSYG-RGADLDGVPQPFHPIPNVP
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   EEEDGVDDLEGEFGLQDGAAHEDDPQYVAESMLRAQMSYG-RGGDAH---PGFSPVPNVP
SEQ ID NO:10  EEEDGVDDLDNEFNW-DG----HDSQSVAESMLYGHMSYG-RGGDPNGAPQAFQLNPNVP
SEQ ID NO:12  ------------------------------------------------------------
SEQ ID NO:14  DEEDV-DDIEHEFNIDEQKNKHGQ---VAEAMLHGRMSYG--RGPEDDDNSQFPTPVIAG
SEQ ID NO:16  ------------------------------------------------------------
SEQ ID NO:18  ------------------------------------------------------------
SEQ ID NO:20  ------------------------------------------------------------
SEQ ID NO:22  -----------------------------------------------------------P
SEQ ID NO:23  DEDDV-DDIENEFNYAQGANKARH---QRHGE---EFSSS--SRHESQPIPLLTHGHTVS
SEQ ID NO:24  EEEEDIDDLEYEFD------HGMDPEHAAEAALSSRLNTG--RGGLDSAPPG----SQIP
SEQ ID NO:25  ------------------------------------------------------------
SEQ ID NO:26  -----IGDLDDD-------------------------TPDYSSGALPLPAPG--------
SEQ ID NO:27  DEEDI-DDIEYEFNIEHEQDKHKH---SAEAMLYGKMSYG--RGPEDDENGRFP-PVIAG
SEQ ID NO:28  ------------------------------------------------------------
SEQ ID NO:29  EEEDDIDDLDNEFEYGN---NGIGFDQVSEGMSISRRNSGFPQSDLDSAPPG----SQIP

              241                                                      300
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   LLTNGQMVDDIPPDQHALVPSFV---GGGGKRIHPLPYADPNLPVQPRSMDPSKDLAAYG
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   LLTNGQMVDDIPPEQHALVPSYMSGGGGGGKRIHPLPFADPNLPVQPRSMDPSKDLAAYG
SEQ ID NO:10  LLTNGQMVDDIPPEQHALVPSFM---GGGGKRIHPLPYADPSLPVQPRSMDPSKDLAAYG
SEQ ID NO:12  ------------------------------------------------------------
SEQ ID NO:14  GRSR-----PVSGEFPISSNAYGDQMLSSSLHKRVHPYPVSEPGSARW-----DEKKXDG
SEQ ID NO:16  ------------------------------------------------------------
SEQ ID NO:18  ------------------------------------------------------------
SEQ ID NO:20  ------------------------------------------------------------
SEQ ID NO:22  LLTNGQMVDDIPPEQHALVPSYMSGGGGGGKRIHPLPFADPNLPVQPRSMDPSKDLAAYG
SEQ ID NO:23  GEIRTPDTQSVRTTSGPLGPSDRNAISSPYIDPR-QPVPVRIVDPSK-------DLNSYG
SEQ ID NO:24  LLTYCDEDADMYSDRHALIVP--PS-TGYGNRVYPAPFTDSSAPPQARSMVPQKDIAEYG
SEQ ID NO:25  ------------------------------------------------------------
SEQ ID NO:26  --------KDQRGNNNNMSMMKRNQNGEFDHNRWLF-----------------ETQGTYG
SEQ ID NO:27  GHS---------GEFPVGG-GYGNG--EHGLHKRVHPYPSSEAGS------------EGG
SEQ ID NO:28  ------------------------------------------------------------
SEQ ID NO:29  LLTYGDEDVEISSDRHALIVP--PSLGGHGNRVHPVSLSDPTVAAHRRLMVPQKDLAVYG

              301                                                      360
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   YGSVAWKERMESWKQKQ-ERMHQTRNDGGGD---------DGDDADLPLM-DEARQPLSR
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   YGSVAWKERMEGWKQKQ-ERLQHVRSEGGGDW--------DGDDADLPLM-DEARQPLSR
SEQ ID NO:10  YGSVAWKERMENWKQRQ-ERMHQTGNDGGGD---------DGDDADLPLM-DEARQQLSR
SEQ ID NO:12  ------------------------------------------------------------
SEQ ID NO:14  -----WKDRMDDWKLQQG-----------------NLGPEPDEDPDAAML-DEARQPLSR
SEQ ID NO:16  ------------------------------------------------------------
SEQ ID NO:18  -------------------------HE---------------------------------
SEQ ID NO:20  ------------------------------------------------------------
SEQ ID NO:22  YGSVAWKERMEGWKQKQ-ERLQHVRSEGGGDW--------DGDDADLPLM-DEARQPLSR
SEQ ID NO:23  LGNVDWKERVEGWKLKQEKNMLQMTGKYHEGKGG-EIEGTGSNGEELQM-ADDTRLPMSR
```

Figure 1 (cont'd.)

```
SEQ ID NO:24  YGSVAWKDRMEVWKRRQGEKLQVIKHEGGNNGRGSN-DDDELDDPDMPMM-DEGRQPLSR
SEQ ID NO:25  ------------------------------------------------------------
SEQ ID NO:26  YGNAYWP---------QDEMYGD--------------DMDEGMRGGMVETADKPWRPLSR
SEQ ID NO:27  -----WRERMDDWKLQHG-----------------NLGPEPDDDPEMGLI-DEARQPLSR
SEQ ID NO:28  ------------------------------------------------------------
SEQ ID NO:29  YGSVAWKDRMEEWKRKQNEKLQVVRHEGDP-------DFEDGDDADFPMM-DEGRQPLSM

              361                                                      420
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   KIPLPSSQINPYRMIIIIRLVVLCFFFHYRVMHPVPDAFALWLISVICEIWFAMSWILDQ
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   KVPISSSRINPYRMIIVIRLVVLGFFFHYRVMHPAKDAFALWLISVICEIWFAMSWILDQ
SEQ ID NO:10  KIPLPSSQINPYRMIIIIRLVVLGFFFHYRVMHPVNDAFALWLISVICEIWFAMSWILDQ
SEQ ID NO:12  ------------------------------------------------------------
SEQ ID NO:14  KVPIASSKINPYRMVIVARLVILAFFLRYRLMNPVHDALGLWLTSIICEIWFAFSWILDQ
SEQ ID NO:16  ------------------------------------------------------------
SEQ ID NO:18  -------------------------------LHPVNDAYGLWLTSVICEIWFAVSWIMDQ
SEQ ID NO:20  ------------------------------------------------------------
SEQ ID NO:22  KVPISSSRINPYRMIIVIRLVVLGFFFHYRVMHPAKDAFALWLISVICEIWFAMSCILDQ
SEQ ID NO:23  VVPIPSSRLTPYRVVIILRLIILCFFLQYRTTHPVKNAYPLWLTSVICEIWFAFSWLLDQ
SEQ ID NO:24  KLPIRSSRINPYRMLILCRLAILGLFFHYRILHPVNDAYGLWLTSVICEIWFAVSWILDQ
SEQ ID NO:25  ------------------------------------------------------------
SEQ ID NO:26  RIPIPAAIISPYRLLIVIRFVVLCFFLTWRIRNPNEDAIWLWLMSIICELWFGFSWILDQ
SEQ ID NO:27  KVPIASSKINPYRMVIVARLVILAVFLRYRLLNPVHDALGLWLTSVICEIWFAVSWILDQ
SEQ ID NO:28  ------------------------------------------------------------
SEQ ID NO:29  KIPIKSSKINPYRMLIVLRLVILGLFFHYRILHPVKDAYALWLISVICEIWFAVSWVLDQ

              421                                                      480
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   FPKWFPIERETYLDRLSLRFDKEGHPS-----QLAPVDFFVSTVDPLKEPPLVTANTVLS
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   FPKWLPIERETYLDRLSLRFDKEGQPS-----QLAPIDFFVSTVDPTKEPPLVTANTVLS
SEQ ID NO:10  FPKWFPIERETYLDRLSLRFDKEGQPS-----QLAPIDFFVSTVDPLKEPPLVTTNTVLS
SEQ ID NO:12  ------------------------------------------------------------
SEQ ID NO:14  FPKWFPIDRETYLDRLSIRYEREGEPN-----MLAPVDVFVSTVDPMKEPPLVTANTVLS
SEQ ID NO:16  ------------------------------------------------------------
SEQ ID NO:18  FPKWYPIQRETYLDRLSLRYEKEGKPS-----ELSSVDVFVSTVDPMKEPPLITANTVLS
SEQ ID NO:20  ------------------------------------------------------------
SEQ ID NO:22  FPKWFPIERETYLDRLSLRFDKEGQPS-----QLAPIDFFVSTVDPTKEPPLVTANTVLS
SEQ ID NO:23  FPKWYPINRETYLDRLAIRYDRDGEPS-----QLVPVDVFVSTVDPLKEPPLVTANTVLS
SEQ ID NO:24  FPKWYPIERETYLDRLSLRYEKEGKPS-----GLAPVDVFVSTVDPLKEPPLITANTVLS
SEQ ID NO:25  ------------------------------------------------------------
SEQ ID NO:26  IPKLCPINRSTDLEVLRDKFDMPSPSNPTGRSDLPGIDLFVSTADPEKEPPLVTANTILS
SEQ ID NO:27  FPKWFPIERETYLDRLSLRYEREGEPN-----MLAPVDVFVSTVDPLKEPPLVTSNTVLS
SEQ ID NO:28  ------------------------------------------------------------
SEQ ID NO:29  FPKWYPIERETYLDRLSLRYEKEGKPS-----GLSPVDVFVSTVDPLKEPPLITANTVLS

              481                                                      540
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   ILSVDYPVDKVSCYVSDDGAAMLTFEALSETSEFAKKWVPFCKRYSLEPRAPEWYFQQ--
SEQ ID NO:6   ------------------------------------H-----------------------
SEQ ID NO:8   ILSVDYPVEKVSCYVSDDGAAMLTFEALSETSEFAKKWVPFSKKFNIEPRAPEWYFQQ--
SEQ ID NO:10  ILSVDYPVDKVSCYVSDDGAAMLTFEALSETSEFAKKWVPFCKRYNIEPRAPEWYFQQ--
SEQ ID NO:12  ILAAGYPAGKVTCYISDDAGAEVTRNAVVEAARFAALWVSFCRKHGVEPRNLEAYFNAGE
SEQ ID NO:14  ILAMDYPVDKISCYISDDGASMCTFESLSETAEFARKWVPFCKKFSIEPRAPEMYFSE--
SEQ ID NO:16  ------------------------------------------------------------
SEQ ID NO:18  ILAVDYPVDKVACYVSDDGAAMLTFEALSETSEFARRWVPFCKKYNIEPRAPEWYFGQ--
```

Figure 1 (cont'd.)

```
SEQ ID NO:20  ------------------------------------------------------------
SEQ ID NO:22  ILSVDYPVEKVSCYVSDDGAAMLTFEALSETSEFAKKWVPFSKKFNIEPRAPEWYFQQ--
SEQ ID NO:23  ILSVDYPVDKVACYVSDDGSAMLTFESLSETAEFAKKWVPFCKKFNIEPRAPEFYFAQ--
SEQ ID NO:24  ILAVDYPVDKVACYVSDDGAAMLTFEALSDTAEFARKWVPFCKKFNIEPRAPEWYFSQ--
SEQ ID NO:25  ---------------------------------RRWVPFCKKHNVEPRAPEFYFNE--
SEQ ID NO:26  ILAVDYPVEKVSCYLSDDGGALLSFEAMAEAASFADLWVPFCRKHNIEPRNPDSYFSL--
SEQ ID NO:27  ILAMDYPVEKISCYVSDDGASMLTFESLSETAEFARKWVPFCKKFSIEPRAPEMYFTL--
SEQ ID NO:28  ----DYPVEKVSCYVSDDGAAMLTFEALSETSEFARKWVPFCKKYNIEPRAPEWYFAQ--
SEQ ID NO:29  ILAVDYPVDKVACYVSDDGAAMLTFEALSETAEFARKWVPFCKKYCIEPRAPEWYFCH--

              541                                                      600
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   ----------KIDYLKDKVAPNFVRERRAMKREYEEFKVRINALVAKAQ-----------
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   ----------KIDYLKDKVAASFVRERRAMKREYEEFKVRINALVAKAQ-----------
SEQ ID NO:10  ----------KIDYLKDKVAANFVRERRAMKREYEEFKVRINALVAKAQ-----------
SEQ ID NO:12  GGGGKAKVVARGSY-RGMAWPELVRDRRRVRREYEEMRLRIDALQAADARRR--------
SEQ ID NO:14  ----------KIDYLKDKVQPTFVKERRAMKREYEEFKVRINALVAKAQ-----------
SEQ ID NO:16  ---------------------------------------------AKAQ-----------
SEQ ID NO:18  ----------KMDYLKNKVHPAFVRERRAMKRDYEEFKVRINSLVATAQ-----------
SEQ ID NO:20  ------------------------------------------------------------
SEQ ID NO:22  ----------KIDYLKDKVAASFVRERRAMKREYEEFKVRINALVAKAQ-----------
SEQ ID NO:23  ----------KIDYLKDKIQPSFVKERRAMKREYEEFKVRINALVAKAQ-----------
SEQ ID NO:24  ----------KMDYLKNKVHPAFVRERRAMKRDYEEFKVKINALVATAQ-----------
SEQ ID NO:25  ----------KIDYLKDKVHPSFVKERRAMKREYEEFKVRINALVAKAQ-----------
SEQ ID NO:26  ----------KIDPTKNKSRIDFVKDRRKIKREYDEFKVRINGLPDSIRRRSDAFNAREE
SEQ ID NO:27  ----------KVDYLQDKVHPTFVKERRAMKREYEEFKVRINAQVAKAS-----------
SEQ ID NO:28  ----------KIDYLKDKVQTSFVKERRAMKREYEEFKVRVNGLVAKAQ-----------
SEQ ID NO:29  ----------KMDYLKNKVHPAFVRERRAMKRDYEEFKVKINALVATAQ-----------

              601                                                      660
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   -----------------KVPEEGWTMQDGTPWPG--------NNVRDHPGMIQVFL---
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   -----------------KVPEEGWTMQDGSPWPG--------NNVRDHPGMIQVFL---
SEQ ID NO:10  -----------------KVPEEGWTMQDGTPWPG--------NNVRDHPGMIQVFL---
SEQ ID NO:12  ----------------------------------------RRGAADDHAGVVQVLIDFA
SEQ ID NO:14  -----------------KVPQGGWIMQDGTPWPG--------NNTKDHPGMIQVFL---
SEQ ID NO:16  -----------------KMPEEGWTMQDGTPWPG--------NNPRDHPGMIQVFL---
SEQ ID NO:18  -----------------KVPEDGWTMQDGTPWPG--------NNVRDHPGMIQVFL---
SEQ ID NO:20  ------------------------------------------------------------
SEQ ID NO:22  -----------------KVPEEGWTMQDGSPWPG--------------------------
SEQ ID NO:23  -----------------KIPEEGWTMQDGTPWPG--------NNTRDHPGMIQVFL---
SEQ ID NO:24  -----------------KVPEEGWTMQDGTPWPG--------NNVRDHPGMIQVFL---
SEQ ID NO:25  -----------------KKPEEGWVMQDGTPWPG--------NNTRDHPGMIQVYL---
SEQ ID NO:26  MKALKQMRESGGDPTEPVKVPKATW-MADGTHWPGTWAASTREHSKGDHAGILQVMLKPP
SEQ ID NO:27  -----------------KVPLEGWIMQDGTPWPG--------NNTKDHPGMIQVFL---
SEQ ID NO:28  -----------------KVPEEGWIMQDGTPWPG--------NNTRDHPGMIQVFL---
SEQ ID NO:29  -----------------KVPEDGWTMQDGTPWPG--------NSVRDHPGMIQVFL---

              661                                                      720
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   ------G-QSGGHDVE----GNELPRLVYVSREKRPGYNHHKKAGAMNALVRVSAVLTNA
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   ------G-QSGGRDVE----GNELPRLVYVSREKRPGYNHHKKAGAMNALVRVSAVLSNA
SEQ ID NO:10  ------G-QSGGLDCE----GNELPRLVYVSREKRPGYNHHKKAGAMNALVRVSAVLTNA
SEQ ID NO:12  GSVPQLGVANGSKLIDVASVDVCLPALVYVCREKRRGHAHHRKAGAMNA-----------
```

Figure 1 (cont'd.)

```
SEQ ID NO:14  ------G-SSGGLDTE----GNQLPRLVYVSREKRPGFQHHKKAGAMNALVRVSAVLTNA
SEQ ID NO:16  ------G-HSGGLDTD----GNELPRLVYVSREKRPGFQHHKKAGAMNALIRVSAVLTNG
SEQ ID NO:18  ------G-QDGVRDVE----GNELPRLVYVSREKRPGFDHHKKAGAMNALVRASAIITNA
SEQ ID NO:20  ------------------------------------------------------------
SEQ ID NO:22  ------------------------------------------------------------
SEQ ID NO:23  ------G-HSGGLDTD----GNELPRLIYVSREKRPGFQHHKKAGAMNALIRVSAVLTNG
SEQ ID NO:24  ------G-HSGVRDTD----GNELPRLVYVSREKRPGFDHHKKAGAMNSLIRVSAVLTNG
SEQ ID NO:25  ------G-SAGALDVD----GKELPRLVYVSREKRPGYQHHKKAGAENALVRVSAVLTNA
SEQ ID NO:26  SSDPLIG-NSDDKVIDFSDTDTRLPMFVYVSREKRPGYDHNKKAGAMNALVRASAILSNG
SEQ ID NO:27  ------G-HSGGFDVE----GHELPRLVYVSREKRPGFQHHKKAGAMNALVRAGVLTNA
SEQ ID NO:28  ------G-QSGGLDAE----GNELPRLVYVSREKRPGFQHHKKAGAMNALVRVAGVLTNA
SEQ ID NO:29  ------G-SDGVRDVE----NNELPRLVYVSREKRPGFDHHKKAGAMNSLIRVSGVLSNA

              721                                                       780
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   PYLLNLDCDHYINNSKAIKEAMCFMMDPLLGKK------VCYVQFPQRFDGIDRHDRYAN
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   AYLLNLDCDHYINNSKAIKEAMCFMMDPLVGKK------VCYVQFPQRFDGIDKNDRYAN
SEQ ID NO:10  PYLLNLDCDHYINNSKAIKEAMCFMMDPLLGKK------VCYVQFPQRFDGIDRHDRYAN
SEQ ID NO:12  PFILDLDCDYYVNNSQALRAGICFMIERGGGGAAEDAGAVAFVQFPQRVDGVDPGDRYAN
SEQ ID NO:14  PFMLNLDCDHYVNNSKAAREAMCFLMDPQTGKK------VCYVQFPQRFDGIDTHDRYAN
SEQ ID NO:16  AYLLNVDCDHYFNNSKALKEAMCFMMDPVLGKK------TCYVQFPQRFDGIDLHDRYAN
SEQ ID NO:18  PYLLNVDCDHYINNSKALREAMCFMMDPQLGKK------VCYVQFPQRFDGIDRHDRYSN
SEQ ID NO:20  -----------------EAMCFLMDPNLGPQ------VCYVQFPQRFDGIDRNDRYAN
SEQ ID NO:22  ------------------------------------------------------------
SEQ ID NO:23  AYLLNVDCDHYFNNSKAIKEAMCFMMDPAIGKK------CCYVQFPQRFDGIDLHDRYAN
SEQ ID NO:24  PYLLNVDCDHYINNSKAIRESMCFMMDPQSGKK------VCYVQFPQRFDGIDRHDRYSN
SEQ ID NO:25  PFILNLDCDHYINNSKAMREAMCFLMDPQFGKK------LCYVQFPQRFDGIDRHDRYAN
SEQ ID NO:26  PFILNLDCDHYIYNCKAVREGMCFMMDRG-GED------ICYIQFPQRFEGIDPSDRYAN
SEQ ID NO:27  PFMLNLDCDHYVNNSKAVREAMCFLMDPQIGKK------VCYVQFPQRFDGIDTNDRYAN
SEQ ID NO:28  AFLLNLDCDHYINNSKALREAMCFLMDPNLGKQ------VCYVQFPQRFDGIDRNDRYAN
SEQ ID NO:29  PYLLNVDCDHYINNSKALREAMCFMMDPQSGKK------ICYVQFPQRFDGIDRHDRYSN

              781                                                       840
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   RNVVFFDINMKGLDGIQGPIYVGTGCVFRRQALYGYDAP---KTKKPPSRTCNCWPKWCI
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   RNVVFFDINMKGLDGIQGPIYVGTGCVFRRQALYGYDAP---KTKKPPSRTCNCWPKWCL
SEQ ID NO:10  RNVVFFDINMKGLDGIQGPIYVGTGCVFRRQALYGYDAP---KTKKPPSRTCNCWPKWCF
SEQ ID NO:12  HNRVLFDCTELGLDGLQGPIYVGTGCLFRRVALYSVDLPR--------------------
SEQ ID NO:14  RNTVFFDINMKGLDGIQGPVYVGTGCVFRRQALYGYNPPKGPK--RPKMVSCDC------
SEQ ID NO:16  RNIVFFDINMKGQDGVQGPVYVGTGCCFNRQALYGYDPVLTEEDLE---------PNIIV
SEQ ID NO:18  RNVVFFDINMKGLDGIQGPIYVGTGCVFRRYALYGYDAP---AKKKPPSKTCNCWPKWCC
SEQ ID NO:20  RNTVFFDINLRGLDGIQGPVYVGTGCVFNRTAIYGYEPPIKAK--K---------PGFLA
SEQ ID NO:22  ------------------------------------------------------------
SEQ ID NO:23  RNIVFFDINMKGLDGIQGPVYVGTGCCFNRQALYGYDPVLTEEDLE---------PNIIV
SEQ ID NO:24  RNVVFFDINMKGLDGIQGPIYVGTGCVFRRQALYGFDAP---KKKKPPGKTCNCWPKWCC
SEQ ID NO:25  RNVVFFDINMLGLDGLQGPVYVGTGCVFNRQALYGYDPPVSEKRPK---MTCDCWPSWCC
SEQ ID NO:26  NNTVFFDGNMRALDGVQGPVYVGTGTMFRRFALYGFDPP---------------------
SEQ ID NO:27  RNTVFFDINMKGLDGIQGPVYVGTGCVFKRQALYGYEPPKGPK--RPKMISCGC------
SEQ ID NO:28  RNTVFFDINLRGLDGIQGPVYVGTGCVFNRTALYGYEPPLKPKHRK---------TGILS
SEQ ID NO:29  RNVVFFDINMKGLDGLQGPIYVGTGCVFRRQALYGFDAP---KKKKGPRKTCNCWPKWCL
```

Figure 1 (cont'd.)

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SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   CCCCFGNRKTKKKTKTSKP-------KFEKIKKLF-KKKENQAPAYALGEIDEA--APG-
SEQ ID NO:6   ------------------------------------------------------------
SEQ ID NO:8   SCCC---SRNKNKKKTTKP-------KTEKKKRLFFKKAENPSPAYALGEIDEG--APG-
SEQ ID NO:10  CCCCFGNRKQKK---TTKP-------KTEKKKLLFFKKEENQSPAYALGEIDEA--APG-
SEQ ID NO:12  ------------------------------------------------------------
SEQ ID NO:14  -CPCFGSRKKYKE----------------------------------KNDANGEAASLKG
SEQ ID NO:16  -KSCCGSRKKGKGGNKK--------YS-DKKKAMGR--TESTVPIFNMEDIEEGVEG--Y
SEQ ID NO:18  LCC--GSRKKKN----ANS-------KKEKKRKV--KHSEASKQIHALENIEAGN--EG-
SEQ ID NO:20  -SLCXG-KKKASKSKKR---------SSDKKKSNKH--VDSSVPVFNLEDIEEGVEGAGF
SEQ ID NO:22  ------------------------------------------------------------
SEQ ID NO:23  -KSCCGSRKKGKSS-KK--------YNYEKRRGINR--SDSNAPLFNMEDIDEGFEG--Y
SEQ ID NO:24  LCC--GLRKKSK----T----------KAKDKKT--NTKETSKQIHALENVDEGVIVPV-
SEQ ID NO:25  -CCCGGSRKKSKKKGEKKGLLGGLLYGKKKKMMGKNYVKKGSAPVFDLEEIEEGLEG--Y
SEQ ID NO:26  -----NPDKLLEKKESETEALTTSDFDPDLDVTQLPKRFGNSTLL---------AESIPI
SEQ ID NO:27  -CPCFGRRRKNKK--------------------------------FSKNDMNGDVAALGG
SEQ ID NO:28  -SLCGGSRKKSSKSSKK---------GSDKKKSGKH--VDSTVPVFNLEDIEEGVEGAGF
SEQ ID NO:29  LCF--GSRKNRK----AKT-------VAADKKK---KNREASKQIHALENIEEGRGHKV-

              901                                                       960
SEQ ID NO:2   ------------------------------------------------------------
SEQ ID NO:4   AENEKASIVNQQKLEKKFGQSSVFVASTLLENGGTLKSASPASLLKEAIHVISCGYEDKT
SEQ ID NO:6   ----------------------------------------------------------ET
SEQ ID NO:8   ADIEKAGIVNQQKLEKKFGQSSVFVASTLLENGGTLKSASPASLLKEAIHVISCGYEDKT
SEQ ID NO:10  AENEKAGIVNQQKLEKKFGQSSVFVTSTLLENGGTLKSASPASLLKEAIHVISCGYEDKT
SEQ ID NO:12  ------------------------------------------------------------
SEQ ID NO:14  MDDDKEVLMSQMNFEKKFGQSSIFVTSTLMEEGGVPPSSSPAALLKEAIHVISCGYEDKT
SEQ ID NO:16  DD-ERTLLMSQKSLEKRFGQSPVFIAATFMEQGGIPPSTNPATLLKEAIHVISCGYEDKT
SEQ ID NO:18  TNNEKTSNLTQTKLEKRFGQSPVFVASTLLDDGGVPHGVSPASLLKEAIQVISCGYEDKT
SEQ ID NO:20  DD-EKSVLMSQMSLEKRFGQSAAFVASTLMEYGGVPQSSTPESLLKEAIHVISCGYEDKS
SEQ ID NO:22  ------------------------------------------------------------
SEQ ID NO:23  DD-ERSILMSQRSVEKRFGQSPVFIAATFMEQGGIPPTTNPATLLKEAIHVISCGYEDKT
SEQ ID NO:24  SNVEKRSEATQLKLEKKFGQSPVFVASAVLQNGGVPRNASPACLLREAIQVISCGYEDKT
SEQ ID NO:25  EELEKSTLMSQKNFEKRFGQSPVFIASTLMENGGLPEGTNSTSLIKEAIHVISCGYEEKT
SEQ ID NO:26  AEFQGRPLADHPAV--KYGRPP----GALR----VPRDPLDATTVAESVSVISCWYEDKT
SEQ ID NO:27  AEGDKEHLMFEMNFEKTFGQSSIFVTSTLMEEGGVPPSSSPAVLLKEAIHVISCGYEDKT
SEQ ID NO:28  DD-EKSLLMSQMSLEKRFGQSAVFVASTLMENGGVPQSATPETLLKEAIHVISCGYEDKT
SEQ ID NO:29  LNVEQSTEAMQMKLQKKYGQSPVFVASARLENGGMARNASPACLLKEAIQVISRGYEDKT

              961                                                      1020
SEQ ID NO:2   -------------HEDILTGFKMHARGWISIYCMPPRPCFKGSAPINLSDRLNQVLRWAL
SEQ ID NO:4   GWGKDIGWIYGSVTEDILTGFKMHCHGWRSIYCIPKRAAFKGSAPLNLSDRLHQVLRWAL
SEQ ID NO:6   EWGKEIGWIYGSVTEDILTGFKMHCRGWKSVYCTPTRPAFKGSAPINLSDRLHQVLRWAL
SEQ ID NO:8   DWGKEIGWIYGSITEDILTGFKMHCHGWRSIYCIPKRPAFKGSAPLNLSDRLHQVLRWAL
SEQ ID NO:10  DWGKEIGWIYGSVTEDILTGFKMHCHGWRSIYCIPKRVAFKGSAPLNLSDRLHQVLRWAL
SEQ ID NO:12  ---------------------------WRP--------------------------RRSL
SEQ ID NO:14  EWGLELGWIYGSITEDILTGFKMHCRGWRSIYCMPKRAAFKGTAPINLSDRLNQVLRWAL
SEQ ID NO:16  EWGKEIGWIYGSVTEDILTGFKMHARGWISIYCMPPRPAFKGSAPINLSDRLNQVLRWAL
SEQ ID NO:18  EWGKEVGWIYGSVTEDILTGFKMHCHGWRSVYCIPKRPAFKGSAPINLSDRLHQVLRWAL
SEQ ID NO:20  EWGTEIGWIYGSVTEDILTGFKMHARGWRSIYCMPKRPAFKGSAPINLSDRLNQVLRWAL
SEQ ID NO:22  ------------------------------------------------------------
SEQ ID NO:23  EWGKEIGWIYGSVTEDILTGFKMHARGWISIYCNPPRPAFKGSAPINLSDRLNQVLRWAL
SEQ ID NO:24  EWGKEIGWIYGSVTEDILTGFKMHCHGWRSVYCMPKRAAFKGSAPINLSDRLHQVLRWAL
SEQ ID NO:25  EWGKEIGWIYGSVTEDILTGFKMHCRGWKSVYCVPKRPAFKGSAPINLSDRLHQVLRWAL
SEQ ID NO:26  EWGDRVGWIYGSVTEDVVTGYRMHNRGWRSVYCITKRDSFRGSAPINLTDRLHQVLRWAT
```

Figure 1 (cont'd.)

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SEQ ID NO:27  EWGTELGWIYGSITEDILTGFKMHCRGWRSIYCMPKRPAFKGSAPINLSDRLNQVLRWAL
SEQ ID NO:28  DWGSEIGWIYGSVTEDILTGFKMHARGWRSIYCMPKRPAFKGSAPINLSDRLNQVLRWAL
SEQ ID NO:29  EWGKEIGWIYGSVTEDILTGSKMHSHGWRHVYCTPKLAAFKGSAPINLSDRLHQVLRWAL

              1021                                                    1080
SEQ ID NO:2   GSVEILFSRHCPIWYNYGG-RLKLLERMAYINTIVYPITSLPLIAYCVLPAICLLTNKFI
SEQ ID NO:4   GSIEIFFSNHCPLWYGYGGG-LKFLERFSYINSIVYPWTSIPLLAYCTLPAICLLTGKFI
SEQ ID NO:6   GSVEIFMSRHCPLWYAYGG-RLKWLERFAYTNTIVYPFTSIPLLAYCTIPAVCLLTGKFI
SEQ ID NO:8   GSVEIFFSKHCPLWYGYGGG-LKFLERFSYINSIVYPWTSIPLLAYCTIPAVCLLTGKFI
SEQ ID NO:10  GSIEIFFSNHCPLWYGYGGG-LKFLERFSYINSIVYPWTSIPLLAYCTLPAICLLTGKFI
SEQ ID NO:12  G---------------------------------------------CRL-----------
SEQ ID NO:14  GSIEIFFSHHCPLWYGFKEKKLKWLERFAYANTTVYPFTSIPLVAYCILPAVCLLTDKFI
SEQ ID NO:16  GSIEIFLSRHCPLWYGYNG-KLKPLMRLAYINTIVYPFTSIPLIAYCTLPAFCLLTNKFI
SEQ ID NO:18  GSVEIFFSRHCPIWYGYGGG-LKLLERFSYINSVVYPWTSLPLLVYCTLPAICLLTGKFI
SEQ ID NO:20  GSVEILFSRHCPLWYGYGG-RLKFLERFAYINTTIYPLTSLPLLVYCILPAICLLTGKFI
SEQ ID NO:22  ------------------------------------------------------------
SEQ ID NO:23  GSIEILLSRHCPIWYGYHG-RLRLLERIAYINTIVYPITSIPLIAYCILPAFCLITDRFI
SEQ ID NO:24  GSVEIFLSRHCPIWYGYGGG-LKWLERFSYINSVVYPWTSLPLIVYCSLPAVCLLTGKFI
SEQ ID NO:25  GSVEIFLSRHCPLWYGYGG-KLKWLERLAYINTIVYPFTSIPLLAYCTIPAVCLLTGKFI
SEQ ID NO:26  GSVEIFFSRNNAI---LASKRLKFLQRLAYLNVGIYPFTSLFLILYCFLPAFSLFSGQFI
SEQ ID NO:27  GSVEIFFSRHSPLWYGYKGGKLKWLERFAYANTTIYPFTSIPLLAYCILPAICLLTDKFI
SEQ ID NO:28  GSVEILFSRHCPIWYGYSG-RLKWLERFAYVNTTIYPVTAIPLLMYCTLPAVCLLTNKFI
SEQ ID NO:29  GSVEIFLSRHCPIWYGYGGG-LKWLERLSYINSVVYPWTSLPLIVYCSLPAICLLTGKFI

              1081                                                    1140
SEQ ID NO:2   IPEISNYAGMFFILMFASIFATGILELRWSGVGIEDWWRNEQFWVIGGTSAHLFAVFQGL
SEQ ID NO:4   TPELNNVASLWFMSLFICIFATSILEMRWSGVGIDDWWRNEQFWVIGGVSSHLFAVFQGL
SEQ ID NO:6   IPTLNNLASIWFIALFLSIIATSVLELRWSGVSIEDWWRNEQFWVIGGVSAHLFAVFQGF
SEQ ID NO:8   TPELTNVASIWFMALFICISVTGILEMRWSGVAIDDWWRNEQFWVIGGVSAHLFAVFQGL
SEQ ID NO:10  TPELNNVASLWFMSLFICIFATSILEMRWSGVGIDDWWRNEQFWVIGGVSSHLFAVFQGL
SEQ ID NO:12  ------------------------------------------------------------
SEQ ID NO:14  MPPISTFAGLYFVALFSSIIATGILELKWSGVSIEEWWRNEQFWVIGGVSAHLFAVIQGL
SEQ ID NO:16  IPEISNFASMWFILLFVSIFTTSILELRWSGVSIEDWWRNEQFWVIGGTSAHLFAVFQGL
SEQ ID NO:18  VPEISNYASLVFMALFISIAATGILEMQWGGVSIDDWWRNEQFWVIGGVSSHLFALFQGL
SEQ ID NO:20  MPEISNLASIWFIALFLSIFATGILEMRWSGVGIDEWWRNEQFWVIGGISAHLFAVFQGL
SEQ ID NO:22  ------------------------------------------------------------
SEQ ID NO:23  IPEISNYASIWFILLFISIAVTGILELRWSGVSIEDWWRNEQFWVIGGTSAHLFAVFQGL
SEQ ID NO:24  VPEISNYAGILFMLMFISIAVTGILEMQWGGVGIDDWWRNEQFWVIGGASSHLFALFQGL
SEQ ID NO:25  IPTLSNLTSVWFLALFLSIIATGVLELRWSGVSIQDWWRNEQFWVIGGVSAHLFAVFQGL
SEQ ID NO:26  VRTLSISFLVYLLMITICLIGLAVLEVKWSGIGLEEWWRNEQWWLISGTSSHLYAVVQGV
SEQ ID NO:27  MPPISTFASLFFISLFMSIIVTGILELRWSGVSIEEWWRNEQFWVIGGISAHLFAVVQGL
SEQ ID NO:28  IPQISNLASIWFISLFLSIFATGILKMKWNGVGIDQWWRNEQFWVIGGVSAHLFAVFQGL
SEQ ID NO:29  VPEISNYASILFMALFSSIAITGILEMQWGKVGIDDWWRNEQFWVIGGVSAHLFALFQGL

              1141                                                    1200
SEQ ID NO:2   LKVLAGIDTNFTVTSKANDEDGD--FAELYVFKWTSLLIPPTTVLVINLVGMVAGISYAI
SEQ ID NO:4   LKVIAGVDTSFTVTSKGGDD--EE-FSELYTFKWTTLLIPPTTLLLLNFIGVVAGISNAI
SEQ ID NO:6   LKVLGGVDTSFTVTSKAAGDEADA-FGDLYLFKWTTLLVPPTTLIIINMVGIVAGVSDAV
SEQ ID NO:8   LKVFAGIDTSFTVTSKAGDD--EE-FSELYTFKWTTLLIPPTTLLLLNFIGVVAGISNAI
SEQ ID NO:10  LKVIAGVDTSFTVTSKGGDD--EE-FSELYTFKWTTLLIPPTTLLLLNFIGVVAGVSNAI
SEQ ID NO:12  ------------------------------------------------------------
SEQ ID NO:14  LKVLAGIDTNFTVTSKATDDE-E--FGELYTFKWTTLLIPPTTILIINIVGVVAGISDAI
SEQ ID NO:16  LKVLAGIDTNFTVTSKASDEDGD--FAELYVFKWTSLLIPPTTVLIVNLVGIVAGVSYAI
SEQ ID NO:18  LKVLAGVNTNFTVTSKAADD--GE-FSELYIFKWTSLLIPPMTLLIMNIVGVVVGISDAI
SEQ ID NO:20  LKVLAGIDTNFTVTSKANDEEGD--FAELYMFKWTTLLIPPTTILIINMVGVVAGTSYAI
SEQ ID NO:22  ------------------------------------------------------------
SEQ ID NO:23  LKVLAGIDTNFTVTSKATDEDGD--FAELYIFKWTALLIPPTTVLLVNLIGIVAGVSYAV
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Figure 1 (cont'd.)

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SEQ ID NO:24   LKVLAGVNTNFTVTSKAADD--GA-FSELYIFKWTTLLIPPTTLLIINIIGVIVGVSDAI
SEQ ID NO:25   LKVLAGVDTNFTVTAKAADDTE---FGELYLFKWTTLLIPPTTLIILNMVGVVAGVSDAI
SEQ ID NO:26   LKVIAGIEISFTLTTKSGGDDNEDIYADLYIVKWSSLMIPPIVIAMVNIIAIVVAFIRTI
SEQ ID NO:27   LKILAGIDTNFTVTSKATDDD-D--FGELYAFKWTTLLIPPTTVLIINIVGVVAGISDAI
SEQ ID NO:28   LKVLAGIDTNFTVTSKASDEDGD--FAELYMFKWTTLLIPPTTLLIINLVGVVAGISYVI
SEQ ID NO:29   LKVLAGVDTNFTVTSKAADD--GE-FSDLYLFKWTSLLIPPMTLLIINVIGVIVGVSDAI

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SEQ ID NO:4    NNGYESWGPLFGKLFFAFWVIVHLYPFLKGLVGRQNRTPTIVIVWSILLASIFSLLWVRI
SEQ ID NO:6    NNGYGSWGPLFGKLFFSFWVIVHLYPFLKGLMGRQNRTPTIVVLWSILLASIFSLVWVRI
SEQ ID NO:8    NNGYESWGPLFGKLFFAFWVIVHLYPFLKGLVGRQNRTPTIVIVWSILLASIFSLLWVRV
SEQ ID NO:10   NNGYESWGPLFGKLFFAFWVIVHLYPFLKGLVGRQNRTPTIVIVWSILLASIFSLLWVRI
SEQ ID NO:12   --------------------------------LGEDER------------------LWSRM
SEQ ID NO:14   NNGYQSWGPLFGKLFFSFWVIVHLYPFLKGLMGRQNRTPTIVVIWSVLLASIFSLLWVRI
SEQ ID NO:16   NSGYQSWGPLFGKLFFAIWVIAHLYPFLKGLLGRQNRTPTIVIVWSVLLASIFSLLWVRI
SEQ ID NO:18   NNGYDSWGPLFGRLFFALWVILHLYPFLKGLLGKQDRMPTIILVWSILLASILTLMWVRI
SEQ ID NO:20   NSGYQSWGPLFGKLFFAFWVIVHLYPFLKGLMGRQNRTPTIVIVWAVLLASIFSLLWVRV
SEQ ID NO:22   ------------------------------------------------------------
SEQ ID NO:23   NSGYQSWGPLFGKLFFALWVIAHLYPFLKGLLGRQNRTPTIVIVWSVLLASIFSLLWVRI
SEQ ID NO:24   SNGYDSWGPLFGRLFFALWVIVHLYPFLKGMLGKQDKMPTIIVVWSILLASILTLLWVRV
SEQ ID NO:25   NNGYGSWGPLFGKLFFAFWVILHLYPFLKGLMGRQNRTPTIVVLWSILLASIFSLVWVRI
SEQ ID NO:26   YQAVPQWSKLIGGAFFSFWVLAHLYPFAKGLMGRRGKTPTIVFVWAGLIAITISLLWTAI
SEQ ID NO:27   NNGYQSWGPLFGKLFFSFWVIVHLYPFLKGLMGRQNRTPTIVVIWSVLLASIFSLLWVRI
SEQ ID NO:28   NSGYQSWGPLFGKLFFAFWVIIHLYPFLKGLMGRQNRTPTIVVVWSILLASIFSLLWVRI
SEQ ID NO:29   SNGYDSWGPLFGRLFFALWVIIHLYPFLKGLLGKQDRMPTIIVVWSILLASILTLLWVRV

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SEQ ID NO:6    DPFIPKAKGPILKP-C-GVEC---
SEQ ID NO:8    DPFLAKSNGPLL--EECGLDCN--
SEQ ID NO:10   DPFLAKDDGPLL--EECGLDCN--
SEQ ID NO:12   KQMVILSGPR--------------
SEQ ID NO:14   DPFVLKTKGPDTKL--CGINC---
SEQ ID NO:16   DPFTSDSNKLT--NGQCGINC---
SEQ ID NO:18   NPFVSRD-GPVL--EICGLNCDES
SEQ ID NO:20   DPFTTRLAGPNI--QTCGINC---
SEQ ID NO:22   ------------------------
SEQ ID NO:23   NPFVDANPNANNFNGKGGVF----
SEQ ID NO:24   NPFVAKG-GPVL--EICGLNCGN-
SEQ ID NO:25   DPFLPKQTGPVLKQ-C-GVEC---
SEQ ID NO:26   NP---NTGPAAAAEGVGGGGFQFP
SEQ ID NO:27   DPFVLKTKGPDTSK--CGINC---
SEQ ID NO:28   DPFTTRVTGPDV--EQCGINC---
SEQ ID NO:29   NPFVAKG-GPIL--EICGLDC--L
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Ile Asn Leu Ser Asp Arg Leu Asn Gln Val Leu Arg Trp Ala Leu Gly
35 40 45

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Ser Val Glu Ile Leu Phe Ser Arg His Cys Pro Ile Trp Tyr Asn Tyr
    50                  55                  60

Gly Gly Arg Leu Lys Leu Leu Glu Arg Met Ala Tyr Ile Asn Thr Ile
65                  70                  75                  80

Val Tyr Pro Ile Thr Ser Leu Pro Leu Ile Ala Tyr Cys Val Leu Pro
                85                  90                  95

Ala Ile Cys Leu Leu Thr Asn Lys Phe Ile Ile Pro Glu Ile Ser Asn
            100                 105                 110

Tyr Ala Gly Met Phe Phe Ile Leu Met Phe Ala Ser Ile Phe Ala Thr
        115                 120                 125

Gly Ile Leu Glu Leu Arg Trp Ser Gly Val Gly Ile Glu Asp Trp Trp
    130                 135                 140

Arg Asn Glu Gln Phe Trp Val Ile Gly Gly Thr Ser Ala His Leu Phe
145                 150                 155                 160

Ala Val Phe Gln Gly Leu Leu Lys Val Leu Ala Gly Ile Asp Thr Asn
                165                 170                 175

Phe Thr Val Thr Ser Lys Ala Asn Asp Glu Asp Gly Asp Phe Ala Glu
            180                 185                 190

Leu Tyr Val Phe Lys Trp Thr Ser Leu Leu Ile Pro Pro Thr Thr Val
        195                 200                 205

Leu Val Ile Asn Leu Val Gly Met Val Ala Gly Ile Ser Tyr Ala Ile
    210                 215                 220

Asn Ser Gly Tyr Gln Ser Trp Gly Pro Leu Phe Gly Lys Leu Phe Phe
225                 230                 235                 240

Ser Ile Trp Val Ile Leu His Leu Tyr Pro Phe Leu Lys Gly Leu Met
                245                 250                 255

Gly Lys Gln Asn Arg Thr Pro Thr Ile Val Ile Val Trp Ser Ile Leu
            260                 265                 270

Leu Ala Ser Ile Phe Ser Leu Leu Trp Val Lys Ile Asp Pro Phe Ile
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Ser Asp Thr Gln Lys Ala Val Ala Met Gly Gln Cys Gly Val Asn Cys
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<212> DNA
<213> Zea mays

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ccgccgccgc cgcacgcacg cttgccccgg gatctggaga tctggtagcg ccagggggat   180
ggaggccagc gccgggctgg tcgccggctc gcacaaccgg aacgagctcg tcgtcatccg   240
ccgcgatggc gagccagggc cgaagcccat ggaccagcgg aacggccagg tgtgccagat   300
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<212> PRT
<213> Zea mays

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Gln Lys Leu Ala Ser Val Ser Leu Pro Leu Pro His Ser Arg Phe Ile
20 25 30

Pro Phe Pro Pro Arg Arg Arg Tyr Arg Arg Arg Arg Thr His Ala Cys
35 40 45

Pro Gly Ile Trp Arg Ser Gly Ser Ala Arg Gly Met Glu Ala Ser Ala
50 55 60

Gly Leu Val Ala Gly Ser His Asn Arg Asn Glu Leu Val Val Ile Arg
65 70 75 80

Arg Asp Gly Glu Pro Gly Pro Lys Pro Met Asp Gln Arg Asn Gly Gln
85 90 95

Val Cys Gln Ile Cys Gly Asp Asp Val Gly Arg Asn Pro Asp Gly Glu
100 105 110

Pro Phe Val Ala Cys Asn Glu Cys Ala Phe Pro Ile Cys Arg Asp Cys
115 120 125

Tyr Glu Tyr Glu Arg Arg Glu Gly Thr Gln Asn Cys Pro Gln Cys Lys
130 135 140

Thr Arg Phe Lys Arg Leu Lys Gly Cys Ala Arg Val Pro Gly Asp Glu
145 150 155 160

Glu Glu Asp Gly Val Asp Asp Leu Glu Asn Glu Phe Asn Trp Ser Asp
165 170 175

Lys His Asp Ser Gln Tyr Leu Ala Glu Ser Met Leu His Ala His Met
180 185 190

Ser Tyr Gly Arg Gly Ala Asp Leu Asp Gly Val Pro Gln Pro Phe His
195 200 205

Pro Ile Pro Asn Val Pro Leu Leu Thr Asn Gly Gln Met Val Asp Asp
210 215 220

Ile Pro Pro Asp Gln His Ala Leu Val Pro Ser Phe Val Gly Gly Gly
225 230 235 240

Gly Lys Arg Ile His Pro Leu Pro Tyr Ala Asp Pro Asn Leu Pro Val
245 250 255

Gln Pro Arg Ser Met Asp Pro Ser Lys Asp Leu Ala Ala Tyr Gly Tyr
260 265 270

Gly Ser Val Ala Trp Lys Glu Arg Met Glu Ser Trp Lys Gln Lys Gln
275 280 285

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Glu Arg Met His Gln Thr Arg Asn Asp Gly Gly Gly Asp Asp Gly Asp
    290                 295                 300

Asp Ala Asp Leu Pro Leu Met Asp Glu Ala Arg Gln Pro Leu Ser Arg
305                 310                 315                 320

Lys Ile Pro Leu Pro Ser Ser Gln Ile Asn Pro Tyr Arg Met Ile Ile
                325                 330                 335

Ile Ile Arg Leu Val Val Leu Cys Phe Phe Phe His Tyr Arg Val Met
            340                 345                 350

His Pro Val Pro Asp Ala Phe Ala Leu Trp Leu Ile Ser Val Ile Cys
        355                 360                 365

Glu Ile Trp Phe Ala Met Ser Trp Ile Leu Asp Gln Phe Pro Lys Trp
    370                 375                 380

Phe Pro Ile Glu Arg Glu Thr Tyr Leu Asp Arg Leu Ser Leu Arg Phe
385                 390                 395                 400

Asp Lys Glu Gly His Pro Ser Gln Leu Ala Pro Val Asp Phe Phe Val
                405                 410                 415

Ser Thr Val Asp Pro Leu Lys Glu Pro Pro Leu Val Thr Ala Asn Thr
            420                 425                 430

Val Leu Ser Ile Leu Ser Val Asp Tyr Pro Val Asp Lys Val Ser Cys
        435                 440                 445

Tyr Val Ser Asp Asp Gly Ala Ala Met Leu Thr Phe Glu Ala Leu Ser
    450                 455                 460

Glu Thr Ser Glu Phe Ala Lys Lys Trp Val Pro Phe Cys Lys Arg Tyr
465                 470                 475                 480

Ser Leu Glu Pro Arg Ala Pro Glu Trp Tyr Phe Gln Gln Lys Ile Asp
                485                 490                 495

Tyr Leu Lys Asp Lys Val Ala Pro Asn Phe Val Arg Glu Arg Arg Ala
            500                 505                 510

Met Lys Arg Glu Tyr Glu Glu Phe Lys Val Arg Ile Asn Ala Leu Val
        515                 520                 525

Ala Lys Ala Gln Lys Val Pro Glu Glu Gly Trp Thr Met Gln Asp Gly
    530                 535                 540

Thr Pro Trp Pro Gly Asn Asn Val Arg Asp His Pro Gly Met Ile Gln
545                 550                 555                 560

Val Phe Leu Gly Gln Ser Gly Gly His Asp Val Glu Gly Asn Glu Leu
                565                 570                 575

Pro Arg Leu Val Tyr Val Ser Arg Glu Lys Arg Pro Gly Tyr Asn His
            580                 585                 590

His Lys Lys Ala Gly Ala Met Asn Ala Leu Val Arg Val Ser Ala Val
        595                 600                 605
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Leu Thr Asn Ala Pro Tyr Leu Leu Asn Leu Asp Cys Asp His Tyr Ile
    610                 615                 620

Asn Asn Ser Lys Ala Ile Lys Glu Ala Met Cys Phe Met Met Asp Pro
625                 630                 635                 640

Leu Leu Gly Lys Lys Val Cys Tyr Val Gln Phe Pro Gln Arg Phe Asp
                645                 650                 655

Gly Ile Asp Arg His Asp Arg Tyr Ala Asn Arg Asn Val Val Phe Phe
            660                 665                 670

Asp Ile Asn Met Lys Gly Leu Asp Gly Ile Gln Gly Pro Ile Tyr Val
        675                 680                 685

Gly Thr Gly Cys Val Phe Arg Arg Gln Ala Leu Tyr Gly Tyr Asp Ala
    690                 695                 700

Pro Lys Thr Lys Lys Pro Pro Ser Arg Thr Cys Asn Cys Trp Pro Lys
705                 710                 715                 720

Trp Cys Ile Cys Cys Cys Cys Phe Gly Asn Arg Lys Thr Lys Lys Lys
                725                 730                 735

Thr Lys Thr Ser Lys Pro Lys Phe Glu Lys Ile Lys Lys Leu Phe Lys
            740                 745                 750

Lys Lys Glu Asn Gln Ala Pro Ala Tyr Ala Leu Gly Glu Ile Asp Glu
        755                 760                 765

Ala Ala Pro Gly Ala Glu Asn Glu Lys Ala Ser Ile Val Asn Gln Gln
    770                 775                 780

Lys Leu Glu Lys Lys Phe Gly Gln Ser Ser Val Phe Val Ala Ser Thr
785                 790                 795                 800

Leu Leu Glu Asn Gly Gly Thr Leu Lys Ser Ala Ser Pro Ala Ser Leu
                805                 810                 815

Leu Lys Glu Ala Ile His Val Ile Ser Cys Gly Tyr Glu Asp Lys Thr
            820                 825                 830

Gly Trp Gly Lys Asp Ile Gly Trp Ile Tyr Gly Ser Val Thr Glu Asp
        835                 840                 845

Ile Leu Thr Gly Phe Lys Met His Cys His Gly Trp Arg Ser Ile Tyr
    850                 855                 860

Cys Ile Pro Lys Arg Ala Ala Phe Lys Gly Ser Ala Pro Leu Asn Leu
865                 870                 875                 880

Ser Asp Arg Leu His Gln Val Leu Arg Trp Ala Leu Gly Ser Ile Glu
                885                 890                 895

Ile Phe Phe Ser Asn His Cys Pro Leu Trp Tyr Gly Tyr Gly Gly Gly
            900                 905                 910

Leu Lys Phe Leu Glu Arg Phe Ser Tyr Ile Asn Ser Ile Val Tyr Pro
        915                 920                 925
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Trp Thr Ser Ile Pro Leu Leu Ala Tyr Cys Thr Leu Pro Ala Ile Cys
    930                 935                 940

Leu Leu Thr Gly Lys Phe Ile Thr Pro Glu Leu Asn Asn Val Ala Ser
945                 950                 955                 960

Leu Trp Phe Met Ser Leu Phe Ile Cys Ile Phe Ala Thr Ser Ile Leu
                965                 970                 975

Glu Met Arg Trp Ser Gly Val Gly Ile Asp Asp Trp Trp Arg Asn Glu
            980                 985                 990

Gln Phe Trp Val Ile Gly Gly Val Ser Ser His Leu Phe Ala Val Phe
        995                 1000                1005

Gln Gly Leu Leu Lys Val Ile Ala Gly Val Asp Thr Ser Phe Thr Val
    1010                1015                1020

Thr Ser Lys Gly Gly Asp Asp Glu Glu Phe Ser Glu Leu Tyr Thr Phe
1025                1030                1035                1040

Lys Trp Thr Thr Leu Leu Ile Pro Pro Thr Thr Leu Leu Leu Leu Asn
                1045                1050                1055

Phe Ile Gly Val Val Ala Gly Ile Ser Asn Ala Ile Asn Asn Gly Tyr
            1060                1065                1070

Glu Ser Trp Gly Pro Leu Phe Gly Lys Leu Phe Phe Ala Phe Trp Val
        1075                1080                1085

Ile Val His Leu Tyr Pro Phe Leu Lys Gly Leu Val Gly Arg Gln Asn
    1090                1095                1100

Arg Thr Pro Thr Ile Val Ile Val Trp Ser Ile Leu Leu Ala Ser Ile
1105                1110                1115                1120

Phe Ser Leu Leu Trp Val Arg Ile Asp Pro Phe Leu Ala Lys Asp Asp
                1125                1130                1135

Gly Pro Leu Leu Glu Glu Cys Gly Leu Asp Cys Asn
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<212> DNA
<213> Zea mays

<400> 5

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<213> Zea mays

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Thr Glu Asp Ile Leu Thr Gly Phe Lys Met His Cys Arg Gly Trp Lys
             20                  25                  30

Ser Val Tyr Cys Thr Pro Thr Arg Pro Ala Phe Lys Gly Ser Ala Pro
         35                  40                  45

Ile Asn Leu Ser Asp Arg Leu His Gln Val Leu Arg Trp Ala Leu Gly
     50                  55                  60

Ser Val Glu Ile Phe Met Ser Arg His Cys Pro Leu Trp Tyr Ala Tyr
 65                  70                  75                  80

Gly Gly Arg Leu Lys Trp Leu Glu Arg Phe Ala Tyr Thr Asn Thr Ile
                 85                  90                  95

Val Tyr Pro Phe Thr Ser Ile Pro Leu Leu Ala Tyr Cys Thr Ile Pro
            100                 105                 110

Ala Val Cys Leu Leu Thr Gly Lys Phe Ile Ile Pro Thr Leu Asn Asn
        115                 120                 125

Leu Ala Ser Ile Trp Phe Ile Ala Leu Phe Leu Ser Ile Ile Ala Thr
    130                 135                 140

Ser Val Leu Glu Leu Arg Trp Ser Gly Val Ser Ile Glu Asp Trp Trp
145                 150                 155                 160

Arg Asn Glu Gln Phe Trp Val Ile Gly Gly Val Ser Ala His Leu Phe
                165                 170                 175

Ala Val Phe Gln Gly Phe Leu Lys Val Leu Gly Gly Val Asp Thr Ser
            180                 185                 190

Phe Thr Val Thr Ser Lys Ala Ala Gly Asp Glu Ala Asp Ala Phe Gly
        195                 200                 205

Asp Leu Tyr Leu Phe Lys Trp Thr Thr Leu Leu Val Pro Pro Thr Thr
    210                 215                 220

Leu Ile Ile Ile Asn Met Val Gly Ile Val Ala Gly Val Ser Asp Ala
225                 230                 235                 240
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Val Asn Asn Gly Tyr Gly Ser Trp Gly Pro Leu Phe Gly Lys Leu Phe
245 250 255

Phe Ser Phe Trp Val Ile Val His Leu Tyr Pro Phe Leu Lys Gly Leu
260 265 270

Met Gly Arg Gln Asn Arg Thr Pro Thr Ile Val Val Leu Trp Ser Ile
275 280 285

Leu Leu Ala Ser Ile Phe Ser Leu Val Trp Val Arg Ile Asp Pro Phe
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Ile Pro Lys Ala Lys Gly Pro Ile Leu Lys Pro Cys Gly Val Glu Cys
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<213> Zea mays

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Pro Pro Glu Gln His Ala Leu Val Pro Ser Tyr Met Ser Gly Gly Gly
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Pro Val Gln Pro Arg Ser Met Asp Pro Ser Lys Asp Leu Ala Ala Tyr
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Asp Gly Asp Asp Ala Asp Leu Pro Leu Met Asp Glu Ala Arg Gln Pro
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Arg Val Met His Pro Ala Lys Asp Ala Phe Ala Leu Trp Leu Ile Ser
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Lys Gln Arg Gln Glu Arg Met His Gln Thr Gly Asn Asp Gly Gly Gly
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Asp Asp Gly Asp Asp Ala Asp Leu Pro Leu Met Asp Glu Ala Arg Gln
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Gln Leu Ser Arg Lys Ile Pro Leu Pro Ser Ser Gln Ile Asn Pro Tyr
260 265 270

Arg Met Ile Ile Ile Ile Arg Leu Val Val Leu Gly Phe Phe Phe His
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Asp His Tyr Ile Asn Asn Ser Lys Ala Ile Lys Glu Ala Met Cys Phe
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Met Met Asp Pro Leu Leu Gly Lys Lys Val Cys Tyr Val Gln Phe Pro
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Gln Arg Phe Asp Gly Ile Asp Arg His Asp Arg Tyr Ala Asn Arg Asn
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Val Val Phe Phe Asp Ile Asn Met Lys Gly Leu Asp Gly Ile Gln Gly
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Pro Ile Tyr Val Gly Thr Gly Cys Val Phe Arg Arg Gln Ala Leu Tyr
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Gly Tyr Asp Ala Pro Lys Thr Lys Lys Pro Pro Ser Arg Thr Cys Asn
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Cys Trp Pro Lys Trp Cys Phe Cys Cys Cys Cys Phe Gly Asn Arg Lys
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Gln Gln Lys Leu Glu Lys Lys Phe Gly Gln Ser Ser Val Phe Val Thr
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Ser Thr Leu Leu Glu Asn Gly Gly Thr Leu Lys Ser Ala Ser Pro Ala
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<213> Oryza sativa

<400> 12

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            20                  25                  30

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        35                  40                  45

Ala Gly Ala Glu Val Thr Arg Asn Ala Val Val Glu Ala Ala Arg Phe
    50                  55                  60

Ala Ala Leu Trp Val Ser Phe Cys Arg Lys His Gly Val Glu Pro Arg
65                  70                  75                  80

Asn Leu Glu Ala Tyr Phe Asn Ala Gly Glu Gly Gly Gly Gly Lys Ala
                85                  90                  95

Lys Val Val Ala Arg Gly Ser Tyr Arg Gly Met Ala Trp Pro Glu Leu
            100                 105                 110

Val Arg Asp Arg Arg Arg Val Arg Arg Glu Tyr Glu Glu Met Arg Leu
        115                 120                 125

Arg Ile Asp Ala Leu Gln Ala Ala Asp Ala Arg Arg Arg Arg Arg Gly
    130                 135                 140

Ala Ala Asp Asp His Ala Gly Val Val Gln Val Leu Ile Asp Phe Ala
145                 150                 155                 160

Gly Ser Val Pro Gln Leu Gly Val Ala Asn Gly Ser Lys Leu Ile Asp
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Val Ala Ser Val Asp Val Cys Leu Pro Ala Leu Val Tyr Val Cys Arg
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Glu Lys Arg Arg Gly His Ala His His Arg Lys Ala Gly Ala Met Asn
195 200 205

Ala Pro Phe Ile Leu Asp Leu Asp Cys Asp Tyr Tyr Val Asn Asn Ser
210 215 220

Gln Ala Leu Arg Ala Gly Ile Cys Phe Met Ile Glu Arg Gly Gly Gly
225 230 235 240

Gly Ala Ala Glu Asp Ala Gly Ala Val Ala Phe Val Gln Phe Pro Gln
245 250 255

Arg Val Asp Gly Val Asp Pro Gly Asp Arg Tyr Ala Asn His Asn Arg
260 265 270

Val Leu Phe Asp Cys Thr Glu Leu Gly Leu Asp Gly Leu Gln Gly Pro
275 280 285

Ile Tyr Val Gly Thr Gly Cys Leu Phe Arg Arg Val Ala Leu Tyr Ser
290 295 300

Val Asp Leu Pro Arg Trp Arg Pro Arg Arg Ser Leu Gly Cys Arg Leu
305 310 315 320

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325 330 335

Leu Ser Gly Pro Arg
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<212> DNA
<213> Glycine max

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Asp Gly Gln Val Cys Glu Ile Cys Gly Asp Gly Val Gly Leu Thr Val
        35                  40                  45

Asp Gly Asp Leu Phe Val Ala Cys Asn Glu Cys Gly Phe Pro Val Cys
    50                  55                  60
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Arg Pro Cys Tyr Glu Tyr Glu Arg Arg Glu Gly Ser His Leu Cys Pro
65 70 75 80

Gln Cys Lys Thr Arg Tyr Lys Arg Leu Lys Gly Ser Pro Arg Val Glu
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Gly Asp Asp Asp Glu Glu Asp Val Asp Asp Ile Glu His Glu Phe Asn
100 105 110

Ile Asp Glu Gln Lys Asn Lys His Gly Gln Val Ala Glu Ala Met Leu
115 120 125

His Gly Arg Met Ser Tyr Gly Arg Gly Pro Glu Asp Asp Asp Asn Ser
130 135 140

Gln Phe Pro Thr Pro Val Ile Ala Gly Gly Arg Ser Arg Pro Val Ser
145 150 155 160

Gly Glu Phe Pro Ile Ser Ser Asn Ala Tyr Gly Asp Gln Met Leu Ser
165 170 175

Ser Ser Leu His Lys Arg Val His Pro Tyr Pro Val Ser Glu Pro Gly
180 185 190

Ser Ala Arg Trp Asp Glu Lys Lys Xaa Asp Gly Trp Lys Asp Arg Met
195 200 205

Asp Asp Trp Lys Leu Gln Gln Gly Asn Leu Gly Pro Glu Pro Asp Glu
210 215 220

Asp Pro Asp Ala Ala Met Leu Asp Glu Ala Arg Gln Pro Leu Ser Arg
225 230 235 240

Lys Val Pro Ile Ala Ser Ser Lys Ile Asn Pro Tyr Arg Met Val Ile
245 250 255

Val Ala Arg Leu Val Ile Leu Ala Phe Phe Leu Arg Tyr Arg Leu Met
260 265 270

Asn Pro Val His Asp Ala Leu Gly Leu Trp Leu Thr Ser Ile Ile Cys
275 280 285

Glu Ile Trp Phe Ala Phe Ser Trp Ile Leu Asp Gln Phe Pro Lys Trp
290 295 300

Phe Pro Ile Asp Arg Glu Thr Tyr Leu Asp Arg Leu Ser Ile Arg Tyr
305 310 315 320

Glu Arg Glu Gly Glu Pro Asn Met Leu Ala Pro Val Asp Val Phe Val
325 330 335

Ser Thr Val Asp Pro Met Lys Glu Pro Pro Leu Val Thr Ala Asn Thr
340 345 350

Val Leu Ser Ile Leu Ala Met Asp Tyr Pro Val Asp Lys Ile Ser Cys
355 360 365

Tyr Ile Ser Asp Asp Gly Ala Ser Met Cys Thr Phe Glu Ser Leu Ser
370 375 380

Glu Thr Ala Glu Phe Ala Arg Lys Trp Val Pro Phe Cys Lys Lys Phe
385 390 395 400

Ser Ile Glu Pro Arg Ala Pro Glu Met Tyr Phe Ser Glu Lys Ile Asp
405 410 415

Tyr Leu Lys Asp Lys Val Gln Pro Thr Phe Val Lys Glu Arg Arg Ala
420 425 430

Met Lys Arg Glu Tyr Glu Glu Phe Lys Val Arg Ile Asn Ala Leu Val
435 440 445

Ala Lys Ala Gln Lys Val Pro Gln Gly Gly Trp Ile Met Gln Asp Gly
450 455 460

Thr Pro Trp Pro Gly Asn Asn Thr Lys Asp His Pro Gly Met Ile Gln
465 470 475 480

Val Phe Leu Gly Ser Ser Gly Gly Leu Asp Thr Glu Gly Asn Gln Leu
485 490 495

Pro Arg Leu Val Tyr Val Ser Arg Glu Lys Arg Pro Gly Phe Gln His
500 505 510

His Lys Lys Ala Gly Ala Met Asn Ala Leu Val Arg Val Ser Ala Val
515 520 525

Leu Thr Asn Ala Pro Phe Met Leu Asn Leu Asp Cys Asp His Tyr Val
530 535 540

Asn Asn Ser Lys Ala Ala Arg Glu Ala Met Cys Phe Leu Met Asp Pro
545 550 555 560

Gln Thr Gly Lys Lys Val Cys Tyr Val Gln Phe Pro Gln Arg Phe Asp
565 570 575

Gly Ile Asp Thr His Asp Arg Tyr Ala Asn Arg Asn Thr Val Phe Phe
580 585 590

Asp Ile Asn Met Lys Gly Leu Asp Gly Ile Gln Gly Pro Val Tyr Val
595 600 605

Gly Thr Gly Cys Val Phe Arg Arg Gln Ala Leu Tyr Gly Tyr Asn Pro
610 615 620

Pro Lys Gly Pro Lys Arg Pro Lys Met Val Ser Cys Asp Cys Cys Pro
625 630 635 640

Cys Phe Gly Ser Arg Lys Lys Tyr Lys Glu Lys Asn Asp Ala Asn Gly
645 650 655

Glu Ala Ala Ser Leu Lys Gly Met Asp Asp Asp Lys Glu Val Leu Met
660 665 670

Ser Gln Met Asn Phe Glu Lys Lys Phe Gly Gln Ser Ser Ile Phe Val
675 680 685

Thr Ser Thr Leu Met Glu Glu Gly Val Pro Pro Ser Ser Ser Pro
690 695 700

Ala Ala Leu Leu Lys Glu Ala Ile His Val Ile Ser Cys Gly Tyr Glu
705 710 715 720

Asp Lys Thr Glu Trp Gly Leu Glu Leu Gly Trp Ile Tyr Gly Ser Ile
725 730 735

Thr Glu Asp Ile Leu Thr Gly Phe Lys Met His Cys Arg Gly Trp Arg
740 745 750

Ser Ile Tyr Cys Met Pro Lys Arg Ala Ala Phe Lys Gly Thr Ala Pro
755 760 765

Ile Asn Leu Ser Asp Arg Leu Asn Gln Val Leu Arg Trp Ala Leu Gly
770 775 780

Ser Ile Glu Ile Phe Phe Ser His His Cys Pro Leu Trp Tyr Gly Phe
785 790 795 800

Lys Glu Lys Lys Leu Lys Trp Leu Glu Arg Phe Ala Tyr Ala Asn Thr
805 810 815

Thr Val Tyr Pro Phe Thr Ser Ile Pro Leu Val Ala Tyr Cys Ile Leu
820 825 830

Pro Ala Val Cys Leu Leu Thr Asp Lys Phe Ile Met Pro Pro Ile Ser
835 840 845

Thr Phe Ala Gly Leu Tyr Phe Val Ala Leu Phe Ser Ser Ile Ile Ala
850 855 860

Thr Gly Ile Leu Glu Leu Lys Trp Ser Gly Val Ser Ile Glu Glu Trp
865 870 875 880

Trp Arg Asn Glu Gln Phe Trp Val Ile Gly Gly Val Ser Ala His Leu
885 890 895

Phe Ala Val Ile Gln Gly Leu Leu Lys Val Leu Ala Gly Ile Asp Thr
900 905 910

Asn Phe Thr Val Thr Ser Lys Ala Thr Asp Asp Glu Glu Phe Gly Glu
915 920 925

Leu Tyr Thr Phe Lys Trp Thr Thr Leu Leu Ile Pro Pro Thr Thr Ile
930 935 940

Leu Ile Ile Asn Ile Val Gly Val Val Ala Gly Ile Ser Asp Ala Ile
945 950 955 960

Asn Asn Gly Tyr Gln Ser Trp Gly Pro Leu Phe Gly Lys Leu Phe Phe
965 970 975

Ser Phe Trp Val Ile Val His Leu Tyr Pro Phe Leu Lys Gly Leu Met
980 985 990

Gly Arg Gln Asn Arg Thr Pro Thr Ile Val Val Ile Trp Ser Val Leu
995 1000 1005

Leu Ala Ser Ile Phe Ser Leu Leu Trp Val Arg Ile Asp Pro Phe Val
1010 1015 1020

Leu Lys Thr Lys Gly Pro Asp Thr Lys Leu Cys Gly Ile Asn Cys
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<213> Glycine max

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Val Phe Leu Gly His Ser Gly Gly Leu Asp Thr Asp Gly Asn Glu Leu
35 40 45

Pro Arg Leu Val Tyr Val Ser Arg Glu Lys Arg Pro Gly Phe Gln His
50 55 60

His Lys Lys Ala Gly Ala Met Asn Ala Leu Ile Arg Val Ser Ala Val
65 70 75 80

Leu Thr Asn Gly Ala Tyr Leu Leu Asn Val Asp Cys Asp His Tyr Phe
85 90 95

Asn Asn Ser Lys Ala Leu Lys Glu Ala Met Cys Phe Met Met Asp Pro
100 105 110

Val Leu Gly Lys Lys Thr Cys Tyr Val Gln Phe Pro Gln Arg Phe Asp
115 120 125

Gly Ile Asp Leu His Asp Arg Tyr Ala Asn Arg Asn Ile Val Phe Phe
130 135 140

Asp Ile Asn Met Lys Gly Gln Asp Gly Val Gln Gly Pro Val Tyr Val
145 150 155 160

Gly Thr Gly Cys Cys Phe Asn Arg Gln Ala Leu Tyr Gly Tyr Asp Pro
165 170 175

Val Leu Thr Glu Glu Asp Leu Glu Pro Asn Ile Ile Val Lys Ser Cys
180 185 190

Cys Gly Ser Arg Lys Lys Gly Lys Gly Gly Asn Lys Lys Tyr Ser Asp
195 200 205

Lys Lys Lys Ala Met Gly Arg Thr Glu Ser Thr Val Pro Ile Phe Asn
210 215 220

Met Glu Asp Ile Glu Glu Gly Val Glu Gly Tyr Asp Asp Glu Arg Thr
225 230 235 240

Leu Leu Met Ser Gln Lys Ser Leu Glu Lys Arg Phe Gly Gln Ser Pro
245 250 255

Val Phe Ile Ala Ala Thr Phe Met Glu Gln Gly Gly Ile Pro Pro Ser
260 265 270

Thr Asn Pro Ala Thr Leu Leu Lys Glu Ala Ile His Val Ile Ser Cys
275 280 285

Gly Tyr Glu Asp Lys Thr Glu Trp Gly Lys Glu Ile Gly Trp Ile Tyr
290 295 300

Gly Ser Val Thr Glu Asp Ile Leu Thr Gly Phe Lys Met His Ala Arg
305 310 315 320

Gly Trp Ile Ser Ile Tyr Cys Met Pro Pro Arg Pro Ala Phe Lys Gly
325 330 335

Ser Ala Pro Ile Asn Leu Ser Asp Arg Leu Asn Gln Val Leu Arg Trp
340 345 350

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Ala Leu Gly Ser Ile Glu Ile Phe Leu Ser Arg His Cys Pro Leu Trp
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Tyr Gly Tyr Asn Gly Lys Leu Lys Pro Leu Met Arg Leu Ala Tyr Ile
    370                 375                 380

Asn Thr Ile Val Tyr Pro Phe Thr Ser Ile Pro Leu Ile Ala Tyr Cys
385                 390                 395                 400

Thr Leu Pro Ala Phe Cys Leu Leu Thr Asn Lys Phe Ile Ile Pro Glu
                405                 410                 415

Ile Ser Asn Phe Ala Ser Met Trp Phe Ile Leu Leu Phe Val Ser Ile
            420                 425                 430

Phe Thr Thr Ser Ile Leu Glu Leu Arg Trp Ser Gly Val Ser Ile Glu
        435                 440                 445

Asp Trp Trp Arg Asn Glu Gln Phe Trp Val Ile Gly Gly Thr Ser Ala
    450                 455                 460

His Leu Phe Ala Val Phe Gln Gly Leu Leu Lys Val Leu Ala Gly Ile
465                 470                 475                 480

Asp Thr Asn Phe Thr Val Thr Ser Lys Ala Ser Asp Glu Asp Gly Asp
                485                 490                 495

Phe Ala Glu Leu Tyr Val Phe Lys Trp Thr Ser Leu Leu Ile Pro Pro
            500                 505                 510

Thr Thr Val Leu Ile Val Asn Leu Val Gly Ile Val Ala Gly Val Ser
        515                 520                 525

Tyr Ala Ile Asn Ser Gly Tyr Gln Ser Trp Gly Pro Leu Phe Gly Lys
    530                 535                 540

Leu Phe Phe Ala Ile Trp Val Ile Ala His Leu Tyr Pro Phe Leu Lys
545                 550                 555                 560

Gly Leu Leu Gly Arg Gln Asn Arg Thr Pro Thr Ile Val Ile Val Trp
                565                 570                 575

Ser Val Leu Leu Ala Ser Ile Phe Ser Leu Leu Trp Val Arg Ile Asp
            580                 585                 590

Pro Phe Thr Ser Asp Ser Asn Lys Leu Thr Asn Gly Gln Cys Gly Ile
        595                 600                 605

Asn Cys
    610

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&lt;211&gt;  2890
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agaaacatac cttgatcgtc tgtcactcag gtatgaaaaa gaagggaagc catctgagtt   180
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<210> 18
<211> 793
<212> PRT
<213> Glycine max

<400> 18

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His Glu Leu His Pro Val Asn Asp Ala Tyr Gly Leu Trp Leu Thr Ser
1               5                   10                  15

Val Ile Cys Glu Ile Trp Phe Ala Val Ser Trp Ile Met Asp Gln Phe
            20                  25                  30
```

```
Pro Lys Trp Tyr Pro Ile Gln Arg Glu Thr Tyr Leu Asp Arg Leu Ser
        35                  40                  45

Leu Arg Tyr Glu Lys Glu Gly Lys Pro Ser Glu Leu Ser Ser Val Asp
    50                  55                  60

Val Phe Val Ser Thr Val Asp Pro Met Lys Glu Pro Pro Leu Ile Thr
65                  70                  75                  80

Ala Asn Thr Val Leu Ser Ile Leu Ala Val Asp Tyr Pro Val Asp Lys
                85                  90                  95

Val Ala Cys Tyr Val Ser Asp Asp Gly Ala Ala Met Leu Thr Phe Glu
            100                 105                 110

Ala Leu Ser Glu Thr Ser Glu Phe Ala Arg Arg Trp Val Pro Phe Cys
        115                 120                 125

Lys Lys Tyr Asn Ile Glu Pro Arg Ala Pro Glu Trp Tyr Phe Gly Gln
    130                 135                 140

Lys Met Asp Tyr Leu Lys Asn Lys Val His Pro Ala Phe Val Arg Glu
145                 150                 155                 160

Arg Arg Ala Met Lys Arg Asp Tyr Glu Glu Phe Lys Val Arg Ile Asn
                165                 170                 175

Ser Leu Val Ala Thr Ala Gln Lys Val Pro Glu Asp Gly Trp Thr Met
            180                 185                 190

Gln Asp Gly Thr Pro Trp Pro Gly Asn Asn Val Arg Asp His Pro Gly
        195                 200                 205

Met Ile Gln Val Phe Leu Gly Gln Asp Gly Val Arg Asp Val Glu Gly
    210                 215                 220

Asn Glu Leu Pro Arg Leu Val Tyr Val Ser Arg Glu Lys Arg Pro Gly
225                 230                 235                 240

Phe Asp His His Lys Lys Ala Gly Ala Met Asn Ala Leu Val Arg Ala
                245                 250                 255

Ser Ala Ile Ile Thr Asn Ala Pro Tyr Leu Leu Asn Val Asp Cys Asp
            260                 265                 270

His Tyr Ile Asn Asn Ser Lys Ala Leu Arg Glu Ala Met Cys Phe Met
        275                 280                 285

Met Asp Pro Gln Leu Gly Lys Lys Val Cys Tyr Val Gln Phe Pro Gln
    290                 295                 300

Arg Phe Asp Gly Ile Asp Arg His Asp Arg Tyr Ser Asn Arg Asn Val
305                 310                 315                 320

Val Phe Phe Asp Ile Asn Met Lys Gly Leu Asp Gly Ile Gln Gly Pro
                325                 330                 335

Ile Tyr Val Gly Thr Gly Cys Val Phe Arg Arg Tyr Ala Leu Tyr Gly
            340                 345                 350
```

```
Tyr Asp Ala Pro Ala Lys Lys Lys Pro Pro Ser Lys Thr Cys Asn Cys
        355                 360                 365

Trp Pro Lys Trp Cys Cys Leu Cys Cys Gly Ser Arg Lys Lys Lys Asn
    370                 375                 380

Ala Asn Ser Lys Lys Glu Lys Lys Arg Lys Val Lys His Ser Glu Ala
385                 390                 395                     400

Ser Lys Gln Ile His Ala Leu Glu Asn Ile Glu Ala Gly Asn Glu Gly
                405                 410                 415

Thr Asn Asn Glu Lys Thr Ser Asn Leu Thr Gln Thr Lys Leu Glu Lys
            420                 425                 430

Arg Phe Gly Gln Ser Pro Val Phe Val Ala Ser Thr Leu Leu Asp Asp
        435                 440                 445

Gly Gly Val Pro His Gly Val Ser Pro Ala Ser Leu Leu Lys Glu Ala
    450                 455                 460

Ile Gln Val Ile Ser Cys Gly Tyr Glu Asp Lys Thr Glu Trp Gly Lys
465                 470                 475                     480

Glu Val Gly Trp Ile Tyr Gly Ser Val Thr Glu Asp Ile Leu Thr Gly
                485                 490                 495

Phe Lys Met His Cys His Gly Trp Arg Ser Val Tyr Cys Ile Pro Lys
            500                 505                 510

Arg Pro Ala Phe Lys Gly Ser Ala Pro Ile Asn Leu Ser Asp Arg Leu
        515                 520                 525

His Gln Val Leu Arg Trp Ala Leu Gly Ser Val Glu Ile Phe Phe Ser
    530                 535                 540

Arg His Cys Pro Ile Trp Tyr Gly Tyr Gly Gly Gly Leu Lys Leu Leu
545                 550                 555                     560

Glu Arg Phe Ser Tyr Ile Asn Ser Val Val Tyr Pro Trp Thr Ser Leu
                565                 570                 575

Pro Leu Leu Val Tyr Cys Thr Leu Pro Ala Ile Cys Leu Leu Thr Gly
            580                 585                 590

Lys Phe Ile Val Pro Glu Ile Ser Asn Tyr Ala Ser Leu Val Phe Met
        595                 600                 605

Ala Leu Phe Ile Ser Ile Ala Ala Thr Gly Ile Leu Glu Met Gln Trp
    610                 615                 620

Gly Gly Val Ser Ile Asp Asp Trp Trp Arg Asn Glu Gln Phe Trp Val
625                 630                 635                     640

Ile Gly Gly Val Ser Ser His Leu Phe Ala Leu Phe Gln Gly Leu Leu
                645                 650                 655

Lys Val Leu Ala Gly Val Asn Thr Asn Phe Thr Val Thr Ser Lys Ala
            660                 665                 670
```

```
Ala Asp Asp Gly Glu Phe Ser Glu Leu Tyr Ile Phe Lys Trp Thr Ser
        675                 680                 685

Leu Leu Ile Pro Pro Met Thr Leu Leu Ile Met Asn Ile Val Gly Val
    690                 695                 700

Val Val Gly Ile Ser Asp Ala Ile Asn Asn Gly Tyr Asp Ser Trp Gly
705                 710                 715                 720

Pro Leu Phe Gly Arg Leu Phe Phe Ala Leu Trp Val Ile Leu His Leu
                725                 730                 735

Tyr Pro Phe Leu Lys Gly Leu Leu Gly Lys Gln Asp Arg Met Pro Thr
            740                 745                 750

Ile Ile Leu Val Trp Ser Ile Leu Leu Ala Ser Ile Leu Thr Leu Met
        755                 760                 765

Trp Val Arg Ile Asn Pro Phe Val Ser Arg Asp Gly Pro Val Leu Glu
    770                 775                 780

Ile Cys Gly Leu Asn Cys Asp Glu Ser
785                 790

<210>  19
<211>  1742
<212>  DNA
<213>  Triticum aestivum

<220>
<221>  unsure
<222>  (9)

<220>
<221>  unsure
<222>  (271)

<400>  19
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actgtctttt ttgatattaa cttgaggggc cttgacggca ttcaaggacc agtttatgtg   180
ggaactggtt gtgttttcaa cagaacggct atctatggtt atgagccccc aattaaggcg   240
aagaagccag gtttcttggc atcattatgt nggggcaaga agaaggcaag caagtcaaag   300
aaaaggagct cagataagaa aaagtcgaac aagcatgtgg acagttctgt tccagtattc   360
aatctcgaag acatagagga gggtgttgaa ggtgctgggt ttgatgatga gaaatcagtt   420
ctcatgtctc aaatgagctt agagaagaga tttggccagt cagcagcatt tgttgcctcc   480
actctgatgg aatatggtgg tgttcctcag tcgtccactc cagaatctct tttgaaagaa   540
gctatccatg tcataagttg tggctatgag gacaagtctg aatggggaac tgagattggt   600
tggatctatg gatctgtcac agaagatatt ctaactggat tcaagatgca cgcaagaggc   660
tggcgttcaa tctattgcat gcccaagcgc ccagctttca agggatctgc ccccatcaat   720
ctttcagatc gtctgaatca agtgctgcgg tgggctcttg gttctgttga aattcttttc   780
agccggcatt gccccttatg gtatggctac ggagggcgcc tcaagttcct ggagagattc   840
gcttacatca acaccaccat ttacccacta acctctctcc cgcttctagt ctattgtata   900
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agtatctggt tcattgcgct cttcctttca attttcgcca ctggtatcct tgagatgagg  1020
tggagtggtg ttggcattga cgagtggtgg aggaatgaac agttctgggt cattggaggt  1080
atctctgccc atctgtttgc cgtctttcag ggtcttctga aggtgcttgc aggtatcgac  1140
accaacttca ctgtcacctc aaaggctaat gatgaagaag gcgactttgc tgagctctac  1200
atgttcaagt ggacgacgct tcttatccct ccgacgacca ttttgatcat taacatggtc  1260
ggtgtcgttg ctggtacctc ctacgccatc aacagtggtt accaatcatg gggccgctc   1320
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tctatcttct ccttgctgtg ggttcgtgtt gatccattca ctacccgtct cgctggccca 1500
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<210> 20
<211> 506
<212> PRT
<213> Triticum aestivum

<220>
<221> UNSURE
<222> (88)

<400> 20

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Tyr Val Gln Phe Pro Gln Arg Phe Asp Gly Ile Asp Arg Asn Asp Arg
            20                  25                  30

Tyr Ala Asn Arg Asn Thr Val Phe Phe Asp Ile Asn Leu Arg Gly Leu
        35                  40                  45

Asp Gly Ile Gln Gly Pro Val Tyr Val Gly Thr Gly Cys Val Phe Asn
    50                  55                  60

Arg Thr Ala Ile Tyr Gly Tyr Glu Pro Pro Ile Lys Ala Lys Lys Pro
65                  70                  75                  80

Gly Phe Leu Ala Ser Leu Cys Xaa Gly Lys Lys Lys Ala Ser Lys Ser
                85                  90                  95

Lys Lys Arg Ser Ser Asp Lys Lys Lys Ser Asn Lys His Val Asp Ser
            100                 105                 110

Ser Val Pro Val Phe Asn Leu Glu Asp Ile Glu Glu Gly Val Glu Gly
        115                 120                 125

Ala Gly Phe Asp Asp Glu Lys Ser Val Leu Met Ser Gln Met Ser Leu
    130                 135                 140

Glu Lys Arg Phe Gly Gln Ser Ala Ala Phe Val Ala Ser Thr Leu Met
145                 150                 155                 160

Glu Tyr Gly Gly Val Pro Gln Ser Ser Thr Pro Glu Ser Leu Leu Lys
                165                 170                 175

Glu Ala Ile His Val Ile Ser Cys Gly Tyr Glu Asp Lys Ser Glu Trp
            180                 185                 190

Gly Thr Glu Ile Gly Trp Ile Tyr Gly Ser Val Thr Glu Asp Ile Leu
        195                 200                 205

Thr Gly Phe Lys Met His Ala Arg Gly Trp Arg Ser Ile Tyr Cys Met
    210                 215                 220
```

Pro Lys Arg Pro Ala Phe Lys Gly Ser Ala Pro Ile Asn Leu Ser Asp
225 230 235 240

Arg Leu Asn Gln Val Leu Arg Trp Ala Leu Gly Ser Val Glu Ile Leu
245 250 255

Phe Ser Arg His Cys Pro Leu Trp Tyr Gly Tyr Gly Gly Arg Leu Lys
260 265 270

Phe Leu Glu Arg Phe Ala Tyr Ile Asn Thr Thr Ile Tyr Pro Leu Thr
275 280 285

Ser Leu Pro Leu Leu Val Tyr Cys Ile Leu Pro Ala Ile Cys Leu Leu
290 295 300

Thr Gly Lys Phe Ile Met Pro Glu Ile Ser Asn Leu Ala Ser Ile Trp
305 310 315 320

Phe Ile Ala Leu Phe Leu Ser Ile Phe Ala Thr Gly Ile Leu Glu Met
325 330 335

Arg Trp Ser Gly Val Gly Ile Asp Glu Trp Trp Arg Asn Glu Gln Phe
340 345 350

Trp Val Ile Gly Gly Ile Ser Ala His Leu Phe Ala Val Phe Gln Gly
355 360 365

Leu Leu Lys Val Leu Ala Gly Ile Asp Thr Asn Phe Thr Val Thr Ser
370 375 380

Lys Ala Asn Asp Glu Glu Gly Asp Phe Ala Glu Leu Tyr Met Phe Lys
385 390 395 400

Trp Thr Thr Leu Leu Ile Pro Pro Thr Thr Ile Leu Ile Ile Asn Met
405 410 415

Val Gly Val Val Ala Gly Thr Ser Tyr Ala Ile Asn Ser Gly Tyr Gln
420 425 430

Ser Trp Gly Pro Leu Phe Gly Lys Leu Phe Phe Ala Phe Trp Val Ile
435 440 445

Val His Leu Tyr Pro Phe Leu Lys Gly Leu Met Gly Arg Gln Asn Arg
450 455 460

Thr Pro Thr Ile Val Ile Val Trp Ala Val Leu Leu Ala Ser Ile Phe
465 470 475 480

Ser Leu Leu Trp Val Arg Val Asp Pro Phe Thr Thr Arg Leu Ala Gly
485 490 495

Pro Asn Ile Gln Thr Cys Gly Ile Asn Cys
500 505

<210> 21
<211> 1029
<212> DNA
<213> Triticum aestivum

<400> 21

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gcacgagccg ctcctcacca acggccagat ggttgatgac atcccgccgg agcagcacgc   60
gctcgtgccg tcctacatga gcggcggcgg cggcgggggc aagaggatcc acccgctccc  120
tttcgcagat cccaaccttc cagtgcaacc gagatccatg gacccgtcca aggatctggc  180
cgcctacgga tatggcagcg tggcctggaa ggagagaatg gagggctgga agcagaagca  240
ggagcgcctg cagcatgtca ggagcgaggg tggcggtgat tgggatggcg acgatgcaga  300
tctgccacta atggatgaag ctaggcagcc attgtccaga aaagtcccta tatcatcaag  360
ccgaattaat ccctacagga tgattatcgt tatccggttg gtggttttgg gtttcttctt  420
ccactaccga gtgatgcatc cggcgaaaga tgcatttgca ttgtggctca tatctgtaat  480
ctgtgaaatc tggtttgcga tgtcctgtat tcttgatcag ttcccaaagt ggtttccaat  540
cgagagagag acttacctgg accgtttgtc actaaggttt gacaaggaag gtcaaccctc  600
tcagcttgct ccaatcgact tctttgtcag tacggttgat cccacaaagg aacctccctt  660
ggtcacagcg aacactgtcc tttccatcct ttctgtggat tatccggttg agaaggtctc  720
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tagggagagg agggcgatga agagagaata cgaggaattc aaggtaagga tcaatgcctt  960
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gcctggaaa                                                          1029
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<210> 22
<211> 340
<212> PRT
<213> Triticum aestivum

<400> 22

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Pro Leu Leu Thr Asn Gly Gln Met Val Asp Asp Ile Pro Pro Glu Gln
1               5                   10                  15

His Ala Leu Val Pro Ser Tyr Met Ser Gly Gly Gly Gly Gly Gly Lys
            20                  25                  30

Arg Ile His Pro Leu Pro Phe Ala Asp Pro Asn Leu Pro Val Gln Pro
        35                  40                  45

Arg Ser Met Asp Pro Ser Lys Asp Leu Ala Ala Tyr Gly Tyr Gly Ser
    50                  55                  60

Val Ala Trp Lys Glu Arg Met Glu Gly Trp Lys Gln Lys Gln Glu Arg
65                  70                  75                  80

Leu Gln His Val Arg Ser Glu Gly Gly Gly Asp Trp Asp Gly Asp Asp
                85                  90                  95

Ala Asp Leu Pro Leu Met Asp Glu Ala Arg Gln Pro Leu Ser Arg Lys
            100                 105                 110

Val Pro Ile Ser Ser Ser Arg Ile Asn Pro Tyr Arg Met Ile Ile Val
        115                 120                 125

Ile Arg Leu Val Val Leu Gly Phe Phe Phe His Tyr Arg Val Met His
    130                 135                 140

Pro Ala Lys Asp Ala Phe Ala Leu Trp Leu Ile Ser Val Ile Cys Glu
145                 150                 155                 160

Ile Trp Phe Ala Met Ser Cys Ile Leu Asp Gln Phe Pro Lys Trp Phe
                165                 170                 175
```

Pro Ile Glu Arg Glu Thr Tyr Leu Asp Arg Leu Ser Leu Arg Phe Asp
180 185 190

Lys Glu Gly Gln Pro Ser Gln Leu Ala Pro Ile Asp Phe Phe Val Ser
195 200 205

Thr Val Asp Pro Thr Lys Glu Pro Pro Leu Val Thr Ala Asn Thr Val
210 215 220

Leu Ser Ile Leu Ser Val Asp Tyr Pro Val Glu Lys Val Ser Cys Tyr
225 230 235 240

Val Ser Asp Asp Gly Ala Ala Met Leu Thr Phe Glu Ala Leu Ser Glu
245 250 255

Thr Ser Glu Phe Ala Lys Lys Trp Val Pro Phe Ser Lys Lys Phe Asn
260 265 270

Ile Glu Pro Arg Ala Pro Glu Trp Tyr Phe Gln Gln Lys Ile Asp Tyr
275 280 285

Leu Lys Asp Lys Val Ala Ala Ser Phe Val Arg Glu Arg Arg Ala Met
290 295 300

Lys Arg Glu Tyr Glu Glu Phe Lys Val Arg Ile Asn Ala Leu Val Ala
305 310 315 320

Lys Ala Gln Lys Val Pro Glu Glu Gly Trp Thr Met Gln Asp Gly Ser
325 330 335

Pro Trp Pro Gly
340

<210> 23
<211> 1081
<212> PRT
<213> Arabidopsis thaliana

<400> 23
Met Glu Ala Ser Ala Gly Leu Val Ala Gly Ser Tyr Arg Arg Asn Glu
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Leu Val Arg Ile Arg His Glu Ser Asp Gly Gly Thr Lys Pro Leu Lys
20 25 30

Asn Met Asn Gly Gln Ile Cys Gln Ile Cys Gly Asp Asp Val Gly Leu
35 40 45

Ala Glu Thr Gly Asp Val Phe Val Ala Cys Asn Glu Cys Ala Phe Pro
50 55 60

Val Cys Arg Pro Cys Tyr Glu Tyr Glu Arg Lys Asp Gly Thr Gln Cys
65 70 75 80

Cys Pro Gln Cys Lys Thr Arg Phe Arg Arg His Arg Gly Ser Pro Arg
85 90 95

Val Glu Gly Asp Glu Asp Glu Asp Asp Val Asp Asp Ile Glu Asn Glu
100 105 110

```
Phe Asn Tyr Ala Gln Gly Ala Asn Lys Ala Arg His Gln Arg His Gly
        115                 120                 125

Glu Glu Phe Ser Ser Ser Ser Arg His Glu Ser Gln Pro Ile Pro Leu
    130                 135                 140

Leu Thr His Gly His Thr Val Ser Gly Glu Ile Arg Thr Pro Asp Thr
145                 150                 155                 160

Gln Ser Val Arg Thr Thr Ser Gly Pro Leu Gly Pro Ser Asp Arg Asn
                165                 170                 175

Ala Ile Ser Ser Pro Tyr Ile Asp Pro Arg Gln Pro Val Pro Val Arg
            180                 185                 190

Ile Val Asp Pro Ser Lys Asp Leu Asn Ser Tyr Gly Leu Gly Asn Val
        195                 200                 205

Asp Trp Lys Glu Arg Val Glu Gly Trp Lys Leu Lys Gln Glu Lys Asn
    210                 215                 220

Met Leu Gln Met Thr Gly Lys Tyr His Glu Gly Lys Gly Gly Glu Ile
225                 230                 235                 240

Glu Gly Thr Gly Ser Asn Gly Glu Glu Leu Gln Met Ala Asp Asp Thr
                245                 250                 255

Arg Leu Pro Met Ser Arg Val Val Pro Ile Pro Ser Ser Arg Leu Thr
            260                 265                 270

Pro Tyr Arg Val Val Ile Ile Leu Arg Leu Ile Ile Leu Cys Phe Phe
        275                 280                 285

Leu Gln Tyr Arg Thr Thr His Pro Val Lys Asn Ala Tyr Pro Leu Trp
    290                 295                 300

Leu Thr Ser Val Ile Cys Glu Ile Trp Phe Ala Phe Ser Trp Leu Leu
305                 310                 315                 320

Asp Gln Phe Pro Lys Trp Tyr Pro Ile Asn Arg Glu Thr Tyr Leu Asp
                325                 330                 335

Arg Leu Ala Ile Arg Tyr Asp Arg Asp Gly Glu Pro Ser Gln Leu Val
            340                 345                 350

Pro Val Asp Val Phe Val Ser Thr Val Asp Pro Leu Lys Glu Pro Pro
        355                 360                 365

Leu Val Thr Ala Asn Thr Val Leu Ser Ile Leu Ser Val Asp Tyr Pro
    370                 375                 380

Val Asp Lys Val Ala Cys Tyr Val Ser Asp Asp Gly Ser Ala Met Leu
385                 390                 395                 400

Thr Phe Glu Ser Leu Ser Glu Thr Ala Glu Phe Ala Lys Lys Trp Val
                405                 410                 415

Pro Phe Cys Lys Lys Phe Asn Ile Glu Pro Arg Ala Pro Glu Phe Tyr
            420                 425                 430
```

Phe Ala Gln Lys Ile Asp Tyr Leu Lys Asp Lys Ile Gln Pro Ser Phe
435 440 445

Val Lys Glu Arg Arg Ala Met Lys Arg Glu Tyr Glu Glu Phe Lys Val
450 455 460

Arg Ile Asn Ala Leu Val Ala Lys Ala Gln Lys Ile Pro Glu Glu Gly
465 470 475 480

Trp Thr Met Gln Asp Gly Thr Pro Trp Pro Gly Asn Asn Thr Arg Asp
485 490 495

His Pro Gly Met Ile Gln Val Phe Leu Gly His Ser Gly Gly Leu Asp
500 505 510

Thr Asp Gly Asn Glu Leu Pro Arg Leu Ile Tyr Val Ser Arg Glu Lys
515 520 525

Arg Pro Gly Phe Gln His His Lys Lys Ala Gly Ala Met Asn Ala Leu
530 535 540

Ile Arg Val Ser Ala Val Leu Thr Asn Gly Ala Tyr Leu Leu Asn Val
545 550 555 560

Asp Cys Asp His Tyr Phe Asn Asn Ser Lys Ala Ile Lys Glu Ala Met
565 570 575

Cys Phe Met Met Asp Pro Ala Ile Gly Lys Lys Cys Cys Tyr Val Gln
580 585 590

Phe Pro Gln Arg Phe Asp Gly Ile Asp Leu His Asp Arg Tyr Ala Asn
595 600 605

Arg Asn Ile Val Phe Phe Asp Ile Asn Met Lys Gly Leu Asp Gly Ile
610 615 620

Gln Gly Pro Val Tyr Val Gly Thr Gly Cys Cys Phe Asn Arg Gln Ala
625 630 635 640

Leu Tyr Gly Tyr Asp Pro Val Leu Thr Glu Glu Asp Leu Glu Pro Asn
645 650 655

Ile Ile Val Lys Ser Cys Cys Gly Ser Arg Lys Lys Gly Lys Ser Ser
660 665 670

Lys Lys Tyr Asn Tyr Glu Lys Arg Arg Gly Ile Asn Arg Ser Asp Ser
675 680 685

Asn Ala Pro Leu Phe Asn Met Glu Asp Ile Asp Glu Gly Phe Glu Gly
690 695 700

Tyr Asp Asp Glu Arg Ser Ile Leu Met Ser Gln Arg Ser Val Glu Lys
705 710 715 720

Arg Phe Gly Gln Ser Pro Val Phe Ile Ala Ala Thr Phe Met Glu Gln
725 730 735

Gly Gly Ile Pro Pro Thr Thr Asn Pro Ala Thr Leu Leu Lys Glu Ala
740 745 750

Ile His Val Ile Ser Cys Gly Tyr Glu Asp Lys Thr Glu Trp Gly Lys
755 760 765

Glu Ile Gly Trp Ile Tyr Gly Ser Val Thr Glu Asp Ile Leu Thr Gly
770 775 780

Phe Lys Met His Ala Arg Gly Trp Ile Ser Ile Tyr Cys Asn Pro Pro
785 790 795 800

Arg Pro Ala Phe Lys Gly Ser Ala Pro Ile Asn Leu Ser Asp Arg Leu
805 810 815

Asn Gln Val Leu Arg Trp Ala Leu Gly Ser Ile Glu Ile Leu Leu Ser
820 825 830

Arg His Cys Pro Ile Trp Tyr Gly Tyr His Gly Arg Leu Arg Leu Leu
835 840 845

Glu Arg Ile Ala Tyr Ile Asn Thr Ile Val Tyr Pro Ile Thr Ser Ile
850 855 860

Pro Leu Ile Ala Tyr Cys Ile Leu Pro Ala Phe Cys Leu Ile Thr Asp
865 870 875 880

Arg Phe Ile Ile Pro Glu Ile Ser Asn Tyr Ala Ser Ile Trp Phe Ile
885 890 895

Leu Leu Phe Ile Ser Ile Ala Val Thr Gly Ile Leu Glu Leu Arg Trp
900 905 910

Ser Gly Val Ser Ile Glu Asp Trp Trp Arg Asn Glu Gln Phe Trp Val
915 920 925

Ile Gly Gly Thr Ser Ala His Leu Phe Ala Val Phe Gln Gly Leu Leu
930 935 940

Lys Val Leu Ala Gly Ile Asp Thr Asn Phe Thr Val Thr Ser Lys Ala
945 950 955 960

Thr Asp Glu Asp Gly Asp Phe Ala Glu Leu Tyr Ile Phe Lys Trp Thr
965 970 975

Ala Leu Leu Ile Pro Pro Thr Thr Val Leu Leu Val Asn Leu Ile Gly
980 985 990

Ile Val Ala Gly Val Ser Tyr Ala Val Asn Ser Gly Tyr Gln Ser Trp
995 1000 1005

Gly Pro Leu Phe Gly Lys Leu Phe Phe Ala Leu Trp Val Ile Ala His
1010 1015 1020

Leu Tyr Pro Phe Leu Lys Gly Leu Leu Gly Arg Gln Asn Arg Thr Pro
1025 1030 1035 1040

Thr Ile Val Ile Val Trp Ser Val Leu Leu Ala Ser Ile Phe Ser Leu
1045 1050 1055

Leu Trp Val Arg Ile Asn Pro Phe Val Asp Ala Asn Pro Asn Ala Asn
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Phe Val Leu Ile Asn Ala Asp Glu Ser Ala Arg Ile Arg Ser Val Gln
            20                  25                  30

Glu Leu Ser Gly Gln Thr Cys Gln Ile Cys Gly Asp Glu Ile Glu Leu
        35                  40                  45

Thr Val Ser Ser Glu Leu Phe Val Ala Cys Asn Glu Cys Ala Phe Pro
    50                  55                  60

Val Cys Arg Pro Cys Tyr Glu Tyr Glu Arg Arg Glu Gly Asn Gln Ala
65                  70                  75                  80

Cys Pro Gln Cys Lys Thr Arg Tyr Lys Arg Ile Lys Gly Ser Pro Arg
                85                  90                  95

Val Asp Gly Asp Asp Glu Glu Glu Glu Asp Ile Asp Asp Leu Glu Tyr
            100                 105                 110

Glu Phe Asp His Gly Met Asp Pro Glu His Ala Ala Glu Ala Ala Leu
        115                 120                 125

Ser Ser Arg Leu Asn Thr Gly Arg Gly Gly Leu Asp Ser Ala Pro Pro
    130                 135                 140

Gly Ser Gln Ile Pro Leu Leu Thr Tyr Cys Asp Glu Asp Ala Asp Met
145                 150                 155                 160

Tyr Ser Asp Arg His Ala Leu Ile Val Pro Pro Ser Thr Gly Tyr Gly
                165                 170                 175

Asn Arg Val Tyr Pro Ala Pro Phe Thr Asp Ser Ser Ala Pro Pro Gln
            180                 185                 190

Ala Arg Ser Met Val Pro Gln Lys Asp Ile Ala Glu Tyr Gly Tyr Gly
        195                 200                 205

Ser Val Ala Trp Lys Asp Arg Met Glu Val Trp Lys Arg Arg Gln Gly
    210                 215                 220

Glu Lys Leu Gln Val Ile Lys His Glu Gly Gly Asn Asn Gly Arg Gly
225                 230                 235                 240

Ser Asn Asp Asp Asp Glu Leu Asp Asp Pro Asp Met Pro Met Met Asp
                245                 250                 255

Glu Gly Arg Gln Pro Leu Ser Arg Lys Leu Pro Ile Arg Ser Ser Arg
            260                 265                 270
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Ile Asn Pro Tyr Arg Met Leu Ile Leu Cys Arg Leu Ala Ile Leu Gly
275 280 285

Leu Phe Phe His Tyr Arg Ile Leu His Pro Val Asn Asp Ala Tyr Gly
290 295 300

Leu Trp Leu Thr Ser Val Ile Cys Glu Ile Trp Phe Ala Val Ser Trp
305 310 315 320

Ile Leu Asp Gln Phe Pro Lys Trp Tyr Pro Ile Glu Arg Glu Thr Tyr
325 330 335

Leu Asp Arg Leu Ser Leu Arg Tyr Glu Lys Glu Gly Lys Pro Ser Gly
340 345 350

Leu Ala Pro Val Asp Val Phe Val Ser Thr Val Asp Pro Leu Lys Glu
355 360 365

Pro Pro Leu Ile Thr Ala Asn Thr Val Leu Ser Ile Leu Ala Val Asp
370 375 380

Tyr Pro Val Asp Lys Val Ala Cys Tyr Val Ser Asp Asp Gly Ala Ala
385 390 395 400

Met Leu Thr Phe Glu Ala Leu Ser Asp Thr Ala Glu Phe Ala Arg Lys
405 410 415

Trp Val Pro Phe Cys Lys Lys Phe Asn Ile Glu Pro Arg Ala Pro Glu
420 425 430

Trp Tyr Phe Ser Gln Lys Met Asp Tyr Leu Lys Asn Lys Val His Pro
435 440 445

Ala Phe Val Arg Glu Arg Arg Ala Met Lys Arg Asp Tyr Glu Glu Phe
450 455 460

Lys Val Lys Ile Asn Ala Leu Val Ala Thr Ala Gln Lys Val Pro Glu
465 470 475 480

Glu Gly Trp Thr Met Gln Asp Gly Thr Pro Trp Pro Gly Asn Asn Val
485 490 495

Arg Asp His Pro Gly Met Ile Gln Val Phe Leu Gly His Ser Gly Val
500 505 510

Arg Asp Thr Asp Gly Asn Glu Leu Pro Arg Leu Val Tyr Val Ser Arg
515 520 525

Glu Lys Arg Pro Gly Phe Asp His His Lys Lys Ala Gly Ala Met Asn
530 535 540

Ser Leu Ile Arg Val Ser Ala Val Leu Ser Asn Ala Pro Tyr Leu Leu
545 550 555 560

Asn Val Asp Cys Asp His Tyr Ile Asn Asn Ser Lys Ala Ile Arg Glu
565 570 575

Ser Met Cys Phe Met Met Asp Pro Gln Ser Gly Lys Lys Val Cys Tyr
580 585 590

Val Gln Phe Pro Gln Arg Phe Asp Gly Ile Asp Arg His Asp Arg Tyr
595 600 605

Ser Asn Arg Asn Val Val Phe Phe Asp Ile Asn Met Lys Gly Leu Asp
610 615 620

Gly Ile Gln Gly Pro Ile Tyr Val Gly Thr Gly Cys Val Phe Arg Arg
625 630 635 640

Gln Ala Leu Tyr Gly Phe Asp Ala Pro Lys Lys Lys Lys Pro Pro Gly
645 650 655

Lys Thr Cys Asn Cys Trp Pro Lys Trp Cys Cys Leu Cys Cys Gly Leu
660 665 670

Arg Lys Lys Ser Lys Thr Lys Ala Lys Asp Lys Lys Thr Asn Thr Lys
675 680 685

Glu Thr Ser Lys Gln Ile His Ala Leu Glu Asn Val Asp Glu Gly Val
690 695 700

Ile Val Pro Val Ser Asn Val Glu Lys Arg Ser Glu Ala Thr Gln Leu
705 710 715 720

Lys Leu Glu Lys Lys Phe Gly Gln Ser Pro Val Phe Val Ala Ser Ala
725 730 735

Val Leu Gln Asn Gly Gly Val Pro Arg Asn Ala Ser Pro Ala Cys Leu
740 745 750

Leu Arg Glu Ala Ile Gln Val Ile Ser Cys Gly Tyr Glu Asp Lys Thr
755 760 765

Glu Trp Gly Lys Glu Ile Gly Trp Ile Tyr Gly Ser Val Thr Glu Asp
770 775 780

Ile Leu Thr Gly Phe Lys Met His Cys His Gly Trp Arg Ser Val Tyr
785 790 795 800

Cys Met Pro Lys Arg Ala Ala Phe Lys Gly Ser Ala Pro Ile Asn Leu
805 810 815

Ser Asp Arg Leu His Gln Val Leu Arg Trp Ala Leu Gly Ser Val Glu
820 825 830

Ile Phe Leu Ser Arg His Cys Pro Ile Trp Tyr Gly Tyr Gly Gly Gly
835 840 845

Leu Lys Trp Leu Glu Arg Phe Ser Tyr Ile Asn Ser Val Val Tyr Pro
850 855 860

Trp Thr Ser Leu Pro Leu Ile Val Tyr Cys Ser Leu Pro Ala Val Cys
865 870 875 880

Leu Leu Thr Gly Lys Phe Ile Val Pro Glu Ile Ser Asn Tyr Ala Gly
885 890 895

Ile Leu Phe Met Leu Met Phe Ile Ser Ile Ala Val Thr Gly Ile Leu
900 905 910

Glu Met Gln Trp Gly Gly Val Gly Ile Asp Asp Trp Trp Arg Asn Glu
915 920 925

Gln Phe Trp Val Ile Gly Gly Ala Ser Ser His Leu Phe Ala Leu Phe
930 935 940

Gln Gly Leu Leu Lys Val Leu Ala Gly Val Asn Thr Asn Phe Thr Val
945 950 955 960

Thr Ser Lys Ala Ala Asp Asp Gly Ala Phe Ser Glu Leu Tyr Ile Phe
965 970 975

Lys Trp Thr Thr Leu Leu Ile Pro Pro Thr Thr Leu Leu Ile Ile Asn
980 985 990

Ile Ile Gly Val Ile Val Gly Val Ser Asp Ala Ile Ser Asn Gly Tyr
995 1000 1005

Asp Ser Trp Gly Pro Leu Phe Gly Arg Leu Phe Phe Ala Leu Trp Val
1010 1015 1020

Ile Val His Leu Tyr Pro Phe Leu Lys Gly Met Leu Gly Lys Gln Asp
1025 1030 1035 1040

Lys Met Pro Thr Ile Ile Val Val Trp Ser Ile Leu Leu Ala Ser Ile
1045 1050 1055

Leu Thr Leu Leu Trp Val Arg Val Asn Pro Phe Val Ala Lys Gly Gly
1060 1065 1070

Pro Val Leu Glu Ile Cys Gly Leu Asn Cys Gly Asn
1075 1080

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Pro Glu Phe Tyr Phe Asn Glu Lys Ile Asp Tyr Leu Lys Asp Lys Val
20 25 30

His Pro Ser Phe Val Lys Glu Arg Arg Ala Met Lys Arg Glu Tyr Glu
35 40 45

Glu Phe Lys Val Arg Ile Asn Ala Leu Val Ala Lys Ala Gln Lys Lys
50 55 60

Pro Glu Glu Gly Trp Val Met Gln Asp Gly Thr Pro Trp Pro Gly Asn
65 70 75 80

Asn Thr Arg Asp His Pro Gly Met Ile Gln Val Tyr Leu Gly Ser Ala
85 90 95

Gly Ala Leu Asp Val Asp Gly Lys Glu Leu Pro Arg Leu Val Tyr Val
100 105 110

Ser Arg Glu Lys Arg Pro Gly Tyr Gln His His Lys Lys Ala Gly Ala
115 120 125

Glu Asn Ala Leu Val Arg Val Ser Ala Val Leu Thr Asn Ala Pro Phe
130 135 140

Ile Leu Asn Leu Asp Cys Asp His Tyr Ile Asn Asn Ser Lys Ala Met
145 150 155 160

Arg Glu Ala Met Cys Phe Leu Met Asp Pro Gln Phe Gly Lys Lys Leu
165 170 175

Cys Tyr Val Gln Phe Pro Gln Arg Phe Asp Gly Ile Asp Arg His Asp
180 185 190

Arg Tyr Ala Asn Arg Asn Val Val Phe Phe Asp Ile Asn Met Leu Gly
195 200 205

Leu Asp Gly Leu Gln Gly Pro Val Tyr Val Gly Thr Gly Cys Val Phe
210 215 220

Asn Arg Gln Ala Leu Tyr Gly Tyr Asp Pro Pro Val Ser Glu Lys Arg
225 230 235 240

Pro Lys Met Thr Cys Asp Cys Trp Pro Ser Trp Cys Cys Cys Cys Cys
245 250 255

Gly Gly Ser Arg Lys Lys Ser Lys Lys Lys Gly Glu Lys Lys Gly Leu
260 265 270

Leu Gly Gly Leu Leu Tyr Gly Lys Lys Lys Lys Met Met Gly Lys Asn
275 280 285

Tyr Val Lys Lys Gly Ser Ala Pro Val Phe Asp Leu Glu Glu Ile Glu
290 295 300

Glu Gly Leu Glu Gly Tyr Glu Glu Leu Glu Lys Ser Thr Leu Met Ser
305 310 315 320

Gln Lys Asn Phe Glu Lys Arg Phe Gly Gln Ser Pro Val Phe Ile Ala
325 330 335

Ser Thr Leu Met Glu Asn Gly Gly Leu Pro Glu Gly Thr Asn Ser Thr
340 345 350

Ser Leu Ile Lys Glu Ala Ile His Val Ile Ser Cys Gly Tyr Glu Glu
355 360 365

Lys Thr Glu Trp Gly Lys Glu Ile Gly Trp Ile Tyr Gly Ser Val Thr
370 375 380

Glu Asp Ile Leu Thr Gly Phe Lys Met His Cys Arg Gly Trp Lys Ser
385 390 395 400

Val Tyr Cys Val Pro Lys Arg Pro Ala Phe Lys Gly Ser Ala Pro Ile
405 410 415

Asn Leu Ser Asp Arg Leu His Gln Val Leu Arg Trp Ala Leu Gly Ser
420 425 430

Val Glu Ile Phe Leu Ser Arg His Cys Pro Leu Trp Tyr Gly Tyr Gly
435 440 445

Gly Lys Leu Lys Trp Leu Glu Arg Leu Ala Tyr Ile Asn Thr Ile Val
450 455 460

Tyr Pro Phe Thr Ser Ile Pro Leu Leu Ala Tyr Cys Thr Ile Pro Ala
465 470 475 480

Val Cys Leu Leu Thr Gly Lys Phe Ile Ile Pro Thr Leu Ser Asn Leu
485 490 495

Thr Ser Val Trp Phe Leu Ala Leu Phe Leu Ser Ile Ile Ala Thr Gly
500 505 510

Val Leu Glu Leu Arg Trp Ser Gly Val Ser Ile Gln Asp Trp Trp Arg
515 520 525

Asn Glu Gln Phe Trp Val Ile Gly Gly Val Ser Ala His Leu Phe Ala
530 535 540

Val Phe Gln Gly Leu Leu Lys Val Leu Ala Gly Val Asp Thr Asn Phe
545 550 555 560

Thr Val Thr Ala Lys Ala Ala Asp Asp Thr Glu Phe Gly Glu Leu Tyr
565 570 575

Leu Phe Lys Trp Thr Thr Leu Leu Ile Pro Pro Thr Thr Leu Ile Ile
580 585 590

Leu Asn Met Val Gly Val Val Ala Gly Val Ser Asp Ala Ile Asn Asn
595 600 605

Gly Tyr Gly Ser Trp Gly Pro Leu Phe Gly Lys Leu Phe Phe Ala Phe
610 615 620

Trp Val Ile Leu His Leu Tyr Pro Phe Leu Lys Gly Leu Met Gly Arg
625 630 635 640

Gln Asn Arg Thr Pro Thr Ile Val Val Leu Trp Ser Ile Leu Leu Ala
645 650 655

Ser Ile Phe Ser Leu Val Trp Val Arg Ile Asp Pro Phe Leu Pro Lys
660 665 670

Gln Thr Gly Pro Val Leu Lys Gln Cys Gly Val Glu Cys
675 680 685

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Tyr Val Ser Leu Ser Arg Asp Asn Ile Glu Leu Ser Gly Glu Leu Ser
35 40 45

Gly Asp Tyr Ser Asn Tyr Thr Val His Ile Pro Pro Thr Pro Asp Asn
50 55 60

Gln Pro Met Ala Thr Lys Ala Glu Glu Gln Tyr Val Ser Asn Ser Leu
65 70 75 80

Phe Thr Gly Gly Phe Asn Ser Val Thr Arg Ala His Leu Met Asp Lys
85 90 95

Val Ile Asp Ser Asp Val Thr His Pro Gln Met Ala Gly Ala Lys Gly
100 105 110

Ser Ser Cys Ala Met Pro Ala Cys Asp Gly Asn Val Met Lys Asp Glu
115 120 125

Arg Gly Lys Asp Val Met Pro Cys Glu Cys Arg Phe Lys Ile Cys Arg
130 135 140

Asp Cys Phe Met Asp Ala Gln Lys Glu Thr Gly Leu Cys Pro Gly Cys
145 150 155 160

Lys Glu Gln Tyr Lys Ile Gly Asp Leu Asp Asp Asp Thr Pro Asp Tyr
165 170 175

Ser Ser Gly Ala Leu Pro Leu Pro Ala Pro Gly Lys Asp Gln Arg Gly
180 185 190

Asn Asn Asn Asn Met Ser Met Met Lys Arg Asn Gln Asn Gly Glu Phe
195 200 205

Asp His Asn Arg Trp Leu Phe Glu Thr Gln Gly Thr Tyr Gly Tyr Gly
210 215 220

Asn Ala Tyr Trp Pro Gln Asp Glu Met Tyr Gly Asp Asp Met Asp Glu
225 230 235 240

Gly Met Arg Gly Gly Met Val Glu Thr Ala Asp Lys Pro Trp Arg Pro
245 250 255

Leu Ser Arg Arg Ile Pro Ile Pro Ala Ala Ile Ile Ser Pro Tyr Arg
260 265 270

Leu Leu Ile Val Ile Arg Phe Val Val Leu Cys Phe Phe Leu Thr Trp
275 280 285

Arg Ile Arg Asn Pro Asn Glu Asp Ala Ile Trp Leu Trp Leu Met Ser
290 295 300

Ile Ile Cys Glu Leu Trp Phe Gly Phe Ser Trp Ile Leu Asp Gln Ile
305 310 315 320

Pro Lys Leu Cys Pro Ile Asn Arg Ser Thr Asp Leu Glu Val Leu Arg
325 330 335

Asp Lys Phe Asp Met Pro Ser Pro Ser Asn Pro Thr Gly Arg Ser Asp
340 345 350

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Leu Pro Gly Ile Asp Leu Phe Val Ser Thr Ala Asp Pro Glu Lys Glu
            355                 360                 365

Pro Pro Leu Val Thr Ala Asn Thr Ile Leu Ser Ile Leu Ala Val Asp
        370                 375                 380

Tyr Pro Val Glu Lys Val Ser Cys Tyr Leu Ser Asp Asp Gly Gly Ala
385                 390                 395                 400

Leu Leu Ser Phe Glu Ala Met Ala Glu Ala Ala Ser Phe Ala Asp Leu
                405                 410                 415

Trp Val Pro Phe Cys Arg Lys His Asn Ile Glu Pro Arg Asn Pro Asp
            420                 425                 430

Ser Tyr Phe Ser Leu Lys Ile Asp Pro Thr Lys Asn Lys Ser Arg Ile
        435                 440                 445

Asp Phe Val Lys Asp Arg Arg Lys Ile Lys Arg Glu Tyr Asp Glu Phe
    450                 455                 460

Lys Val Arg Ile Asn Gly Leu Pro Asp Ser Ile Arg Arg Arg Ser Asp
465                 470                 475                 480

Ala Phe Asn Ala Arg Glu Glu Met Lys Ala Leu Lys Gln Met Arg Glu
                485                 490                 495

Ser Gly Gly Asp Pro Thr Glu Pro Val Lys Val Pro Lys Ala Thr Trp
            500                 505                 510

Met Ala Asp Gly Thr His Trp Pro Gly Thr Trp Ala Ala Ser Thr Arg
        515                 520                 525

Glu His Ser Lys Gly Asp His Ala Gly Ile Leu Gln Val Met Leu Lys
    530                 535                 540

Pro Pro Ser Ser Asp Pro Leu Ile Gly Asn Ser Asp Asp Lys Val Ile
545                 550                 555                 560

Asp Phe Ser Asp Thr Asp Thr Arg Leu Pro Met Phe Val Tyr Val Ser
                565                 570                 575

Arg Glu Lys Arg Pro Gly Tyr Asp His Asn Lys Lys Ala Gly Ala Met
            580                 585                 590

Asn Ala Leu Val Arg Ala Ser Ala Ile Leu Ser Asn Gly Pro Phe Ile
        595                 600                 605

Leu Asn Leu Asp Cys Asp His Tyr Ile Tyr Asn Cys Lys Ala Val Arg
    610                 615                 620

Glu Gly Met Cys Phe Met Met Asp Arg Gly Gly Glu Asp Ile Cys Tyr
625                 630                 635                 640

Ile Gln Phe Pro Gln Arg Phe Glu Gly Ile Asp Pro Ser Asp Arg Tyr
                645                 650                 655

Ala Asn Asn Asn Thr Val Phe Phe Asp Gly Asn Met Arg Ala Leu Asp
            660                 665                 670
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Gly Val Gln Gly Pro Val Tyr Val Gly Thr Gly Thr Met Phe Arg Arg
675 680 685

Phe Ala Leu Tyr Gly Phe Asp Pro Pro Asn Pro Asp Lys Leu Leu Glu
690 695 700

Lys Lys Glu Ser Glu Thr Glu Ala Leu Thr Thr Ser Asp Phe Asp Pro
705 710 715 720

Asp Leu Asp Val Thr Gln Leu Pro Lys Arg Phe Gly Asn Ser Thr Leu
725 730 735

Leu Ala Glu Ser Ile Pro Ile Ala Glu Phe Gln Gly Arg Pro Leu Ala
740 745 750

Asp His Pro Ala Val Lys Tyr Gly Arg Pro Pro Gly Ala Leu Arg Val
755 760 765

Pro Arg Asp Pro Leu Asp Ala Thr Thr Val Ala Glu Ser Val Ser Val
770 775 780

Ile Ser Cys Trp Tyr Glu Asp Lys Thr Glu Trp Gly Asp Arg Val Gly
785 790 795 800

Trp Ile Tyr Gly Ser Val Thr Glu Asp Val Val Thr Gly Tyr Arg Met
805 810 815

His Asn Arg Gly Trp Arg Ser Val Tyr Cys Ile Thr Lys Arg Asp Ser
820 825 830

Phe Arg Gly Ser Ala Pro Ile Asn Leu Thr Asp Arg Leu His Gln Val
835 840 845

Leu Arg Trp Ala Thr Gly Ser Val Glu Ile Phe Phe Ser Arg Asn Asn
850 855 860

Ala Ile Leu Ala Ser Lys Arg Leu Lys Phe Leu Gln Arg Leu Ala Tyr
865 870 875 880

Leu Asn Val Gly Ile Tyr Pro Phe Thr Ser Leu Phe Leu Ile Leu Tyr
885 890 895

Cys Phe Leu Pro Ala Phe Ser Leu Phe Ser Gly Gln Phe Ile Val Arg
900 905 910

Thr Leu Ser Ile Ser Phe Leu Val Tyr Leu Leu Met Ile Thr Ile Cys
915 920 925

Leu Ile Gly Leu Ala Val Leu Glu Val Lys Trp Ser Gly Ile Gly Leu
930 935 940

Glu Glu Trp Trp Arg Asn Gln Gln Trp Trp Leu Ile Ser Gly Thr Ser
945 950 955 960

Ser His Leu Tyr Ala Val Val Gln Gly Val Leu Lys Val Ile Ala Gly
965 970 975

Ile Glu Ile Ser Phe Thr Leu Thr Thr Lys Ser Gly Gly Asp Asp Asn
980 985 990

Glu Asp Ile Tyr Ala Asp Leu Tyr Ile Val Lys Trp Ser Ser Leu Met
995 1000 1005

Ile Pro Pro Ile Val Ile Ala Met Val Asn Ile Ile Ala Ile Val Val
1010 1015 1020

Ala Phe Ile Arg Thr Ile Tyr Gln Ala Val Pro Gln Trp Ser Lys Leu
1025 1030 1035 1040

Ile Gly Gly Ala Phe Phe Ser Phe Trp Val Leu Ala His Leu Tyr Pro
1045 1050 1055

Phe Ala Lys Gly Leu Met Gly Arg Arg Gly Lys Thr Pro Thr Ile Val
1060 1065 1070

Phe Val Trp Ala Gly Leu Ile Ala Ile Thr Ile Ser Leu Leu Trp Thr
1075 1080 1085

Ala Ile Asn Pro Asn Thr Gly Pro Ala Ala Ala Ala Glu Gly Val Gly
1090 1095 1100

Gly Gly Gly Phe Gln Phe Pro
1105 1110

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Asp Gly Gln Phe Cys Glu Ile Cys Gly Asp Gln Ile Gly Leu Thr Val
35 40 45

Glu Gly Asp Leu Phe Val Ala Cys Asn Glu Cys Gly Phe Pro Ala Cys
50 55 60

Arg Pro Cys Tyr Glu Tyr Glu Arg Arg Glu Gly Thr Gln Asn Cys Pro
65 70 75 80

Gln Cys Lys Thr Arg Tyr Lys Arg Leu Arg Gly Ser Pro Arg Val Glu
85 90 95

Gly Asp Glu Asp Glu Glu Asp Ile Asp Asp Ile Glu Tyr Glu Phe Asn
100 105 110

Ile Glu His Glu Gln Asp Lys His Lys His Ser Ala Glu Ala Met Leu
115 120 125

Tyr Gly Lys Met Ser Tyr Gly Arg Gly Pro Glu Asp Asp Glu Asn Gly
130 135 140

Arg Phe Pro Pro Val Ile Ala Gly Gly His Ser Gly Glu Phe Pro Val
145 150 155 160

Gly Gly Gly Tyr Gly Asn Gly Glu His Gly Leu His Lys Arg Val His
165 170 175

Pro Tyr Pro Ser Ser Glu Ala Gly Ser Glu Gly Gly Trp Arg Glu Arg
180 185 190

Met Asp Asp Trp Lys Leu Gln His Gly Asn Leu Gly Pro Glu Pro Asp
195 200 205

Asp Asp Pro Glu Met Gly Leu Ile Asp Glu Ala Arg Gln Pro Leu Ser
210 215 220

Arg Lys Val Pro Ile Ala Ser Ser Lys Ile Asn Pro Tyr Arg Met Val
225 230 235 240

Ile Val Ala Arg Leu Val Ile Leu Ala Val Phe Leu Arg Tyr Arg Leu
245 250 255

Leu Asn Pro Val His Asp Ala Leu Gly Leu Trp Leu Thr Ser Val Ile
260 265 270

Cys Glu Ile Trp Phe Ala Val Ser Trp Ile Leu Asp Gln Phe Pro Lys
275 280 285

Trp Phe Pro Ile Glu Arg Glu Thr Tyr Leu Asp Arg Leu Ser Leu Arg
290 295 300

Tyr Glu Arg Glu Gly Glu Pro Asn Met Leu Ala Pro Val Asp Val Phe
305 310 315 320

Val Ser Thr Val Asp Pro Leu Lys Glu Pro Pro Leu Val Thr Ser Asn
325 330 335

Thr Val Leu Ser Ile Leu Ala Met Asp Tyr Pro Val Glu Lys Ile Ser
340 345 350

Cys Tyr Val Ser Asp Asp Gly Ala Ser Met Leu Thr Phe Glu Ser Leu
355 360 365

Ser Glu Thr Ala Glu Phe Ala Arg Lys Trp Val Pro Phe Cys Lys Lys
370 375 380

Phe Ser Ile Glu Pro Arg Ala Pro Glu Met Tyr Phe Thr Leu Lys Val
385 390 395 400

Asp Tyr Leu Gln Asp Lys Val His Pro Thr Phe Val Lys Glu Arg Arg
405 410 415

Ala Met Lys Arg Glu Tyr Glu Glu Phe Lys Val Arg Ile Asn Ala Gln
420 425 430

Val Ala Lys Ala Ser Lys Val Pro Leu Glu Gly Trp Ile Met Gln Asp
435 440 445

Gly Thr Pro Trp Pro Gly Asn Asn Thr Lys Asp His Pro Gly Met Ile
450 455 460

Gln Val Phe Leu Gly His Ser Gly Gly Phe Asp Val Glu Gly His Glu
465 470 475 480

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Leu Pro Arg Leu Val Tyr Val Ser Arg Glu Lys Arg Pro Gly Phe Gln
                485                 490                 495

His His Lys Lys Ala Gly Ala Met Asn Ala Leu Val Arg Val Ala Gly
            500                 505                 510

Val Leu Thr Asn Ala Pro Phe Met Leu Asn Leu Asp Cys Asp His Tyr
        515                 520                 525

Val Asn Asn Ser Lys Ala Val Arg Glu Ala Met Cys Phe Leu Met Asp
    530                 535                 540

Pro Gln Ile Gly Lys Lys Val Cys Tyr Val Gln Phe Pro Gln Arg Phe
545                 550                 555                 560

Asp Gly Ile Asp Thr Asn Asp Arg Tyr Ala Asn Arg Asn Thr Val Phe
                565                 570                 575

Phe Asp Ile Asn Met Lys Gly Leu Asp Gly Ile Gln Gly Pro Val Tyr
            580                 585                 590

Val Gly Thr Gly Cys Val Phe Lys Arg Gln Ala Leu Tyr Gly Tyr Glu
        595                 600                 605

Pro Pro Lys Gly Pro Lys Arg Pro Lys Met Ile Ser Cys Gly Cys Cys
    610                 615                 620

Pro Cys Phe Gly Arg Arg Arg Lys Asn Lys Lys Phe Ser Lys Asn Asp
625                 630                 635                 640

Met Asn Gly Asp Val Ala Ala Leu Gly Gly Ala Glu Gly Asp Lys Glu
                645                 650                 655

His Leu Met Phe Glu Met Asn Phe Glu Lys Thr Phe Gly Gln Ser Ser
            660                 665                 670

Ile Phe Val Thr Ser Thr Leu Met Glu Glu Gly Gly Val Pro Pro Ser
        675                 680                 685

Ser Ser Pro Ala Val Leu Leu Lys Glu Ala Ile His Val Ile Ser Cys
    690                 695                 700

Gly Tyr Glu Asp Lys Thr Glu Trp Gly Thr Glu Leu Gly Trp Ile Tyr
705                 710                 715                 720

Gly Ser Ile Thr Glu Asp Ile Leu Thr Gly Phe Lys Met His Cys Arg
                725                 730                 735

Gly Trp Arg Ser Ile Tyr Cys Met Pro Lys Arg Pro Ala Phe Lys Gly
            740                 745                 750

Ser Ala Pro Ile Asn Leu Ser Asp Arg Leu Asn Gln Val Leu Arg Trp
        755                 760                 765

Ala Leu Gly Ser Val Glu Ile Phe Phe Ser Arg His Ser Pro Leu Trp
    770                 775                 780

Tyr Gly Tyr Lys Gly Gly Lys Leu Lys Trp Leu Glu Arg Phe Ala Tyr
785                 790                 795                 800
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Ala Asn Thr Thr Ile Tyr Pro Phe Thr Ser Ile Pro Leu Leu Ala Tyr
805 810 815

Cys Ile Leu Pro Ala Ile Cys Leu Leu Thr Asp Lys Phe Ile Met Pro
820 825 830

Pro Ile Ser Thr Phe Ala Ser Leu Phe Phe Ile Ser Leu Phe Met Ser
835 840 845

Ile Ile Val Thr Gly Ile Leu Glu Leu Arg Trp Ser Gly Val Ser Ile
850 855 860

Glu Glu Trp Trp Arg Asn Glu Gln Phe Trp Val Ile Gly Gly Ile Ser
865 870 875 880

Ala His Leu Phe Ala Val Val Gln Gly Leu Leu Lys Ile Leu Ala Gly
885 890 895

Ile Asp Thr Asn Phe Thr Val Thr Ser Lys Ala Thr Asp Asp Asp Asp
900 905 910

Phe Gly Glu Leu Tyr Ala Phe Lys Trp Thr Thr Leu Leu Ile Pro Pro
915 920 925

Thr Thr Val Leu Ile Ile Asn Ile Val Gly Val Val Ala Gly Ile Ser
930 935 940

Asp Ala Ile Asn Asn Gly Tyr Gln Ser Trp Gly Pro Leu Phe Gly Lys
945 950 955 960

Leu Phe Phe Ser Phe Trp Val Ile Val His Leu Tyr Pro Phe Leu Lys
965 970 975

Gly Leu Met Gly Arg Gln Asn Arg Thr Pro Thr Ile Val Val Ile Trp
980 985 990

Ser Val Leu Leu Ala Ser Ile Phe Ser Leu Leu Trp Val Arg Ile Asp
995 1000 1005

Pro Phe Val Leu Lys Thr Lys Gly Pro Asp Thr Ser Lys Cys Gly Ile
1010 1015 1020

Asn Cys
1025

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Ala Met Leu Thr Phe Glu Ala Leu Ser Glu Thr Ser Glu Phe Ala Arg
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Lys Trp Val Pro Phe Cys Lys Lys Tyr Asn Ile Glu Pro Arg Ala Pro
35 40 45

Glu Trp Tyr Phe Ala Gln Lys Ile Asp Tyr Leu Lys Asp Lys Val Gln
50 55 60

Thr Ser Phe Val Lys Glu Arg Arg Ala Met Lys Arg Glu Tyr Glu Glu
65 70 75 80

Phe Lys Val Arg Val Asn Gly Leu Val Ala Lys Ala Gln Lys Val Pro
85 90 95

Glu Glu Gly Trp Ile Met Gln Asp Gly Thr Pro Trp Pro Gly Asn Asn
100 105 110

Thr Arg Asp His Pro Gly Met Ile Gln Val Phe Leu Gly Gln Ser Gly
115 120 125

Gly Leu Asp Ala Glu Gly Asn Glu Leu Pro Arg Leu Val Tyr Val Ser
130 135 140

Arg Glu Lys Arg Pro Gly Phe Gln His His Lys Lys Ala Gly Ala Met
145 150 155 160

Asn Ala Leu Val Arg Val Ser Ala Val Leu Thr Asn Gly Ala Phe Leu
165 170 175

Leu Asn Leu Asp Cys Asp His Tyr Ile Asn Asn Ser Lys Ala Leu Arg
180 185 190

Glu Ala Met Cys Phe Leu Met Asp Pro Asn Leu Gly Lys Gln Val Cys
195 200 205

Tyr Val Gln Phe Pro Gln Arg Phe Asp Gly Ile Asp Arg Asn Asp Arg
210 215 220

Tyr Ala Asn Arg Asn Thr Val Phe Phe Asp Ile Asn Leu Arg Gly Leu
225 230 235 240

Asp Gly Ile Gln Gly Pro Val Tyr Val Gly Thr Gly Cys Val Phe Asn
245 250 255

Arg Thr Ala Leu Tyr Gly Tyr Glu Pro Pro Leu Lys Pro Lys His Arg
260 265 270

Lys Thr Gly Ile Leu Ser Ser Leu Cys Gly Gly Ser Arg Lys Lys Ser
275 280 285

Ser Lys Ser Ser Lys Lys Gly Ser Asp Lys Lys Lys Ser Gly Lys His
290 295 300

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<213>  Arabidopsis thaliana

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Pro Cys Tyr Glu Tyr Glu Arg Arg Glu Gly Asn Gln Ala Cys Pro Gln
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Cys Lys Thr Arg Phe Lys Arg Leu Lys Gly Ser Pro Arg Val Glu Gly
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Asp Glu Glu Glu Asp Asp Ile Asp Asp Leu Asp Asn Glu Phe Glu Tyr
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Pro Ile Tyr Val Gly Thr Gly Cys Val Phe Arg Arg Gln Ala Leu Tyr
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Gly Phe Asp Ala Pro Lys Lys Lys Lys Gly Pro Arg Lys Thr Cys Asn
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Cys Trp Pro Lys Trp Cys Leu Leu Cys Phe Gly Ser Arg Lys Asn Arg
660 665 670

Lys Ala Lys Thr Val Ala Ala Asp Lys Lys Lys Lys Asn Arg Glu Ala
675 680 685

Ser Lys Gln Ile His Ala Leu Glu Asn Ile Glu Glu Gly Arg Gly His
690 695 700

Lys Val Leu Asn Val Glu Gln Ser Thr Glu Ala Met Gln Met Lys Leu
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Gly Lys Glu Ile Gly Trp Ile Tyr Gly Ser Val Thr Glu Asp Ile Leu
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820 825 830

Leu Ser Arg His Cys Pro Ile Trp Tyr Gly Tyr Gly Gly Gly Leu Lys
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Trp Leu Glu Arg Leu Ser Tyr Ile Asn Ser Val Val Tyr Pro Trp Thr
850 855 860

Ser Leu Pro Leu Ile Val Tyr Cys Ser Leu Pro Ala Ile Cys Leu Leu
865 870 875 880

Thr Gly Lys Phe Ile Val Pro Glu Ile Ser Asn Tyr Ala Ser Ile Leu
885 890 895

Phe Met Ala Leu Phe Ser Ser Ile Ala Ile Thr Gly Ile Leu Glu Met
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            1060                    1065                    1070

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(54) Title: PLANT CELLULOSE SYNTHASES

(57) Abstract

This invention relates to an isolated nucleic acid fragment encoding a cellulose synthase. The invention also relates to the construction of a chimeric gene encoding all or a portion of the cellulose synthase, in sense or antisense orientation, wherein expression of the chimeric gene results in production of altered levels of the cellulose synthase in a transformed host cell.

```
             1                                                          60
SEQ ID NO:2  ------------------------------------------------------------
SEQ ID NO:4  RAAQAQRNKGKPQPEEQKLASVSLP--LPHSRFIPPPRRRYRRR---RTHACPG----I
SEQ ID NO:6  ------------------------------------------------------------
SEQ ID NO:8  HSSYTKSRSSLAQPRAAPRQAQPPP--ATAACACERSPRPGDQRRGGLRAPRCAAAAGFV
SEQ ID NO:10 ------------------------------------------------------------
SEQ ID NO:12 RCS---RRNTCSSPPPTPTRSRRSPRRTP-------------------------------
SEQ ID NO:14 ------------------------------------------------------------
SEQ ID NO:16 ------------------------------------------------------------
SEQ ID NO:18 ------------------------------------------------------------
SEQ ID NO:20 ------------------------------------------------------------
SEQ ID NO:22 ------------------------------------------------------------
SEQ ID NO:23 ------------------------------------------------------------
SEQ ID NO:24 MNTGGR------------------------------------------------------
SEQ ID NO:25 ------------------------------------------------------------
SEQ ID NO:26 MASTPPQTSKKVRNNSGSGQTVKFARRTSSGRYVSLS-RDNIELSGELSGDYSNYTVHIP
SEQ ID NO:27 ------------------------------------------------------------
SEQ ID NO:28 ------------------------------------------------------------
SEQ ID NO:29 R---PR------------------------------------------------------

             61                                                        120
SEQ ID NO:2  ------------------------------------------------------------
SEQ ID NO:4  M-RSGSARG----ME-ASAGLVAGSHNRNELV-VIRRDGEPGPKP--MDQRNGQVCQI--
SEQ ID NO:6  ------------------------------------------------------------
SEQ ID NO:8  RERDPAGRGGGPEME-ASAGLVAGSHNRNELV-VIRRDRESGAAGGGAARRAEAPCQI--
SEQ ID NO:10 -------------ME-ASAGLVAGSHNRNELV-VIRRDGDPGPKP--PREQNGQVCQI--
SEQ ID NO:12 -------------------------------------------------------C----
SEQ ID NO:14 -------------ME-ASAGLVAGSHNRNELV-VIHGHEEP--KA--LKNLDGQVCEI--
SEQ ID NO:16 ------------------------------------------------------------
SEQ ID NO:18 ------------------------------------------------------------
SEQ ID NO:20 ------------------------------------------------------------
SEQ ID NO:22 ------------------------------------------------------------
SEQ ID NO:23 -------------ME-ASAGLVAGSYRRNELV-RIRHESDGGTKP--LKNMNGQICQI--
SEQ ID NO:24 --------------------LIAGSHNRNEFV-LI--NADESARIRSVQELSGQTCQI--
SEQ ID NO:25 ------------------------------------------------------------
SEQ ID NO:26 PTPDNQPMATKAEEQYVSNSLFTGGFNSVTRAHLMDKVIDSDVTHPQMAGAKGSSCAMPA
SEQ ID NO:27 -------------ME-ASAGLVAGSHNRNELV-VIHNHEEP--KP--LKNLDGQFCEI--
SEQ ID NO:28 ------------------------------------------------------------
SEQ ID NO:29 --------------------LIAGSHNRNEFV-LI--NADEMARIRSVQELSGQTCQI--

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SEQ ID NO:6  ------------------------------------------------------------
SEQ ID NO:8  CGDEVGVGPDGEPFVACNECAFPVCRACYEYERREGSQACPQCKTRYKRLKGCPRVAGD-
SEQ ID NO:10 CGDDVGLAPGGDPFVACNECAFPVCRDCYEYERREGTQNCPQCKTRYKRLKGCQRVTGD-
SEQ ID NO:12 -------------------CPY--------------------------------------
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SEQ ID NO:16 ------------------------------------------------------------
SEQ ID NO:18 ------------------------------------------------------------
SEQ ID NO:20 ------------------------------------------------------------
SEQ ID NO:22 ------------------------------------------------------------
SEQ ID NO:23 CGDDVGLAETGDVFVACNECAFPVCRPCYEYERKDGTQCCPQCKTRFRRHRGSPRVEGDE
SEQ ID NO:24 CGDEIELTVSSELFVACNECAFPVCRPCYEYERREGNQACPQCKTRYKRIKGSPRVDGDD
SEQ ID NO:25 ------------------------------------------------------------
SEQ ID NO:26 CDGNVMKDERGKDVMPC-ECRFKICRDCFMDAQKE-TGLCPGCKEQYK------------
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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/54 C12N1/21 C12N9/10 C12Q1/48 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 00549 A (WILLIAMSON RICHARD EDWARD ;PENG LIANGCAI (AU); ARIOLI ANTONIO (AU)) 8 January 1998 (1998-01-08) see SEQ ID NOs:1-12 ---	1,2,4-7, 10-17

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
9 February 2000	23. 02. 00

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Maddox, A

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ARIOLI, T., ET AL.: "Arabidopsis thaliana cellulose synthase catalytic subunit (RSW1) gene complete cds" EMBL ACCESSION NO:AF027172, 3 February 1998 (1998-02-03), XP002124282 the whole document	1,4-6, 13-17
X	-& ARIOLI, T. ET AL.: "Molecular analysis of cellulose biosynthesis in Arabidopsis" SCIENCE, vol. 279, 30 January 1998 (1998-01-30), pages 717-720, XP002124283 the whole document & ARIOLI, T., ET AL.: "Cellulose synthase catalytic subunit" TREMBL ACCESSION NO:048946, 1 June 1998 (1998-06-01), ---	6,13-17
X	ARIOLI, T., ET AL.: "Arabidopsis thaliana cellulose synthase catalytic subunit (Ath-A) mRNA, complete cds" EMBL ACCESSION NO: AF027173, 3 February 1998 (1998-02-03), XP002129994 the whole document	7,10-17
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WU, L., ET AL.: "Arabidopsis thalaina cellulose synthase mRNA, partial cds" EMBL ACCESSION NO: AF062485, 18 May 1998 (1998-05-18), XP002129995 the whole document -& WU, L., ET AL.: "AraxCelA, a new member of cellulose synthase gene family from Arabidopsis thaliana (accession no. AF062485) (PGR 98-113)" PLANT PHYSIOLOGY 117:1125, July 1998 (1998-07), XP002130048 ---	7,10-17
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 00551 A (MAYO FOUNDATION ;MCDONALD JOHN A (US); SPICER ANDREW P (US); AUGUS) 8 January 1998 (1998-01-08) see page 14 lines 21 and 22, and SEQ ID NO:48	6
P,X	EP 0 875 575 A (NISSHIN SPINNING) 4 November 1998 (1998-11-04) the whole document	1,2,4-7, 10-12
P,X	SASAKI, T., ET AL.: "Oryza sativa cDNA, partial sequence (R2825_6A)." EMBL ACCESSION NO:AU031954, 19 October 1998 (1998-10-19), XP002129999 the whole document	16,17
P,X	TAYLOR, N.G., ET AL.: "Arabidopsis thaliana cellulose synthase catalytic subunit (IRX3) mRNA, complete cds." EMBL ACCESSION NO:AF088917, 25 May 1999 (1999-05-25), XP002130000 the whole document	1,2,6, 16,17
P,X	BLEWITT, M., ET AL.: "BNLGHi13827 Six-day Cotton fiber Gossypium hirsutum cDNA 5' similar to (AF027172) cellulose synthase catalytic subunit [Arabidopsis thaliana] gi¦4049343¦gnl¦PID¦e1361041 (AL034567) cellulose synthase catalytic subunit (RSW1) [Arabidopsis thaliana], mRNA sequence." EMBL ACCESSION NO:AI729626, 12 June 1999 (1999-06-12), XP002130001 the whole document	1,2,6, 16,17
P,X	BLEWITT, M., ET AL.: "BNLGHi5835 Six-day Cotton fiber Gossypium hirsutum cDNA 5' similar to (AF027172) cellulose synthase catalytic subunit [Arabidopsis thaliana] gi¦4049343¦gnl¦PID¦e1361041 (AL034567) cellulose synthase catalytic subunit (RSW1) [Arabidopsis thaliana], mRNA sequence." EMBL ACCESSION NO:AI729981, 12 June 1999 (1999-06-12), XP002130002 the whole document	1,2,6, 16,17
P,X	LAOSINCHAI W., ET AL.: "Gossypium hirsutum cellulose synthase catalytic subunit (celA3) mRNA, complete cds." EMBL ACCESSION NO:AF150630, 21 June 1999 (1999-06-21), XP002130003 the whole document	1,2,6, 16,17

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 723 764 A (SINGLETARY GEORGE WILLIAM ET AL) 3 March 1998 (1998-03-03) ---	13
A	AMOR Y ET AL: "EVIDENCE FOR A CYCLIC DIGUANYLIC ACID-DEPENDENT CELLULOSE SYNTHASE IN PLANTS" PLANT CELL,US,AMERICAN SOCIETY OF PLANT PHYSIOLOGISTS, ROCKVILLE, MD, vol. 3, page 989-995 XP002061420 ISSN: 1040-4651 the whole document ---	6,18
A	LI ET AL: "beta-Glucan synthesis in the cotton fiber" PLANT PHYSIOLOGY,US,AMERICAN SOCIETY OF PLANT PHYSIOLOGISTS, ROCKVILLE, MD, vol. 101, no. 4, page 1149-1156 XP002087180 ISSN: 0032-0889 the whole document ---	6,18
A	WO 91 13988 A (UNIV TEXAS) 19 September 1991 (1991-09-19) the whole document -----	1-6, 13-18

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/15871

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheets

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-6,13-18 all partially

   Nucleic acid fragments encoding barley cellulose synthase,and corresponding polypeptide as represented by SEQ ID NOs:1 and 2, fragments encoding amino acid sequence 90% identical thereto,transformed hosts containing andmethods for obtaining said sequences,methods for altering expression and methods for evaluating inhibitors using said sequences.

2. Claims: 1-6,13-18 all partially and 7-12 all completely

   Nucleic acid fragments encoding corn cellulose synthase,and corresponding polypeptide as represented by SEQ ID NOs:3-10, fragments encoding amino acid sequence 90% identical thereto,transformed hosts containing and methods for obtaining said sequences,methods for altering expression and methods for evaluating inhibitors using said sequences.

3. Claims: 1-6,13-18 all partially

   Nucleic acid fragments encoding rice cellulose synthase,and corresponding polypeptide as represented by SEQ ID NOs:11 and 12, fragments encoding amino acid sequence 90% identical thereto,transformed hosts containing and methods for obtaining said sequences,methods for altering expression and methods for evaluating inhibitors using said sequences.

4. Claims: 1-6,13-18 all partially

   Nucleic acid fragments encoding soybean cellulose synthase,and corresponding polypeptide as represented by SEQ ID NOs:13-18, fragments encoding amino acid sequence 90% identical thereto,transformed hosts containing and methods for obtaining said sequences,methods for altering expression and methods for evaluating inhibitors using said sequences.

5. Claims: 1-6,13-18 all partially

   Nucleic acid fragments encoding wheat cellulose synthase,and corresponding polypeptide as represented by SEQ ID NOs:19-22, fragments encoding amino acid sequence 90% identical thereto,transformed hosts containing and methods for obtaining said sequences,methods for altering expression and methods for evaluating inhibitors using said sequences.

6. Claim : 18 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method for evaluating a compound for inhibitory actívty on cellulose synthase comparing activity of cellulose synthase produced in a transformed host with and without the addition of the compound, not covered by any of the previous groups of claimed inventions 1-5.

INTERNATIONAL SEARCH REPORT

formation on patent family members

International Application No
PL., US 99/15871

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			CA	2259126 A	08-01-1998
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